JUL 28 1928

VOLUME 36 NUMBER 1

AMERICAN JOURNAL OF DISEASES OF CHILDREN

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JULY, 1928

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $5.00

Entered as Second-Class Matter, January 4, 1911, at the Postoffice at Chicago, Illinois, Under Act of Congress of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized on June 14, 1918.

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AMERICAN JOURNAL

OF

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VOLUME 36

1928

PUBLISHERS
AMERICAN MEDICAL ASSOCIATION
CHICAGO, ILL.

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Medical
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PEDIATRICS OF ONE HUNDRED YEARS AGO*

JOHN C. GITTINGS, M.D.
PHILADELPHIA

In his hours of relaxation, it is interesting for the physician occasionally to wander into the philosophical byways which offer opportunities for quiet reflection on medicine as a whole: its ends and aims, its pitfalls and dangers, its methods and standards and its accomplishments.

In this vein it seems desirable to consider the trend of morbidity in childhood, particularly with a view to evaluating the results of efforts for prevention and the lines along which future effort should be directed.

The first logical step requires a familiarity with pediatrics of the past and with the causes of its morbidity and mortality. Most pediatricians have dipped lightly into the pools of ancient knowledge, and all are familiar with the reputation credited to the authors of old of being past-masters in the observation and recording of clinical phenomena. In individual instances, this reputation is warranted, but in general, the outstanding and inevitable conclusion to be drawn from their works is that their ignorance of the basic sciences of medicine, as they are known today, was so profound that with all their art and artistry they could not record reliable conclusions. It is, of course, possible to recognize in their descriptions many diseases which are familiar, but to attach any statistical value to such subjects as are compassed under the title of remittent fever, for example, is impossible.

Mortality statistics of 100 years ago are available, but they were compounded in England at least, largely of laymen's diagnoses. To secure a proper perspective of the past seemed well-nigh hopeless.

As a sample of mortality statistics, Robertson publishes a table of 2,056 deaths of children under 10 years as they were listed in the register of the Rusholme Road Cemetery. Abstracting only those which exceeded forty in number, I find:

	Deaths		Deaths
Convulsions and fits	350	Inflammation of the lungs	155
Measles	299	Chin cough (pertussis)	150
Infantile decline	260	Bowel complaints	125
Smallpox	187	Water on brain	125
Teething	181	Croup (diphtheria)	41

Hamilton sagely notes that convulsions precede death in most diseases of infancy. Even that hardly explains such a large percentage (17 per

* Received for publication, April 30, 1928.

* Presidential Address read before the American Pediatric Society, Washington, D. C., April 30, 1928.

cent), and tetany probably played a conspicuous rôle in this mortality. It is impossible to evaluate infantile decline and teething as causes of death, but of the remaining causes, infection must have been the chief one.

As evidence of what could be done at that time in a proper environment with probably a minimum of exposure to contagion, I find that in the Ackworth Seminary, harboring children from 6 or 8 to 14 years of age, the mortality from disease among 300 inmates over a period of four years was only 3, and at the Cheetham School only 3 deaths occurred among 80 children in twenty-eight years, while at the Warrington Blue Coat School, among 24 scholars there were no deaths in twelve years.

The older literature, however, furnishes a wealth of material of another kind, some instructive, more interesting and most perhaps amusing. Instead of discussing the trend of morbidity, I shall use this, therefore, as an aperitif for the intellectual feast which is to follow.

One is prone to believe that knowledge of child-hygiene has been acquired only in modern times, and yet in 1829, Dewees, whose book on the "Physical and Medical Treatment of Children" went through nine editions, devoted 246 of 517 pages to such sensible instruction in physical care that comparatively little need be added or subtracted today. Other books, such as those of Syer, Haden and Combe, written primarily for mothers, were excellent counterparts of modern products.

That much of the mortality in infancy was due to the parents' ignorance, vice or economic ills is frequently emphasized. Buchan suggests that "if it were made the interest of the poor to keep their children alive by means of state premiums, more lives would be saved than if the whole revenue of the crown were expended on hospitals for that purpose." This last sounds strangely familiar!

Robertson explains graphically some of the conditions to which Buchan refers. During the taking of the census in Glasgow in 1798, a house in the slum district was found in which the hall was filled to the depth of several inches with a putrid fluid, full of maggots, which had flowed in from an adjacent slaughter house. Thirty-seven persons lived in this sty, filth and stench seemed congenial to them. "If they could answer the calls of hunger, they felt, or seemed to feel, nothing else as an inconvenience."

Fresh air was esteemed as highly as it is today. In 1767, an Act of Parliament was passed compelling the parish officers of London and Westminster to send the infants of the poor to the country to be nursed. Prior to this enactment, the mortality among the infants ran as high as 96 per cent. In the year following, it was approximately 16 per cent.

In the matter of exercise, they were not handicapped by fear of bacteria. Underwood advocates allowing infants to crawl on the floor

near the open window or door rather than to be compelled to lie on their backs or to sit upright pinned in chairs. Most authors mention the undoubted value of brisk rubbing of infants with the hand or flesh brush, two or three times a day. This certainly is not advocated today, possibly to the modern infant's detriment.

Modern psychiatry is not so modern after all. Most of the old books of any pretension devote considerable space to the moral management of children, in which a creditable knowledge is displayed of child psychology. Haden states that it is a sure sign of bad moral management when an infant cries before strangers. The modern proponents of the art of training can hardly do better than that! And as to the inculcation of good habits, Robertson believes that whereas the diaper cannot be altogether dispensed with, yet by the end of the third or fourth month, if the nurse be capable, its use can be entirely omitted.

In the principles of successful feeding of infants, the ancients were well grounded. They advocated conservation of breast feeding, dilution of cow's milk with thin gruels for the young infant, milk as fresh as possible, scrupulous cleanliness in the preparation of the formulae and placing of the nipples in spirits when not in use. In 1836, Evanson and Mansell prescribed four hour intervals between feedings and in 1833, Eberle advocated complemental feeding with prolonged intervals for infants with colic and indigestion.

The London authors particularly decried the inability or unwillingness of women of the upper and middle ranks of society to suckle their infants. Then, as now, they were theorizing as to the causes of failure of the milk supply, and ascribed it to deficiency of fresh air and exercise, improper diet and late hours. How much more is known today? In decrying the custom of ladies of fashion to neglect their duties, John Clarke emphasizes the cumulative effect of an example. He tells the story of the courtiers who in compliment to their sovereign, sat down with great caution to imitate him because he was afflicted with piles. Clarke also takes issue with the husband who, from a vitiated mind, is averse to his wife's nursing her own offspring. If he induces his wife to break one of the strongest ties of nature, he has but small right to complain if she is not rigid in observing others that are weaker.

The employment of wet-nurses was universal, and the secret of the abundant supply is explained by Haden. Some of them were married, but they were recruited chiefly from among "those unfortunate young women whose chastity had fallen a sacrifice to the persevering acts of designing men."

Finally as a challenge to the modernist, there is a chapter devoted by Haden to the preschool child!

It is difficult to conceive of a state of mind completely ignorant of the existence of bacterial life, and yet the effect of bacterial activity

was inevitably recognized; for example, the fact that the contents of the body cavities of the new-born infant become acrid as soon as air is admitted. It required a Pasteur to elucidate this mystery.

The epidemiology of infectious diseases was too obvious to be missed, but at this period smallpox and possibly scarlet fever were the only diseases admittedly contagious.

The fallacy in the reasoning does not seem so preposterous when one considers that miasms and atmospheric changes were considered so potent. Dewees speaks of an "epidemic peculiarity of the atmosphere." If the disease is air-borne, contagion need not be invoked. Practically all authors insist that real croup or "cyanche trachealis" occurs only in a damp cold state of the atmosphere, and no one seems to have found any evidence that it was ever transmitted from sick to well persons. If two or three cases occur in one household, are not all the children exposed to the same exciting cause? Measles cannot be traced from house to house and from street to street as in smallpox or scarlet fever, hence it cannot be contagious (Condie). Eberle notes that inoculation has been successfully practiced in measles, but Dewees combats this with even more extensive negative experiments. Condie admits that stomatitis has apparently been transmitted through the medium of a wet-nurse, but claims that it could equally well have been due to a vitiated condition of the nurse's milk. Diarrhea which corresponded to the dysentery of today was due to indigestion, or to bile which is "too great in quantity or highly depraved in quality." Even when contagion was prevented by hygiene, its significance was not recognized. Ventilation of the stifling, overcrowded maternity wards resulted in an immediate and significant decrease in infant mortality; yet the deaths had been ascribed merely to the debilitating effects of bad air.

CHILDREN TREATED BY HEROIC MEASURES

The use, or rather the abuse of drugs, chiefly cathartics, is a source of never-ending wonder![1] The records speak for themselves. A new-born infant became drowsy on the second day; it would not nurse, and for the next six days, insensibility alternated with crying and convulsions. There had not been any free evacuation, so Underwood, in the next thirty-six hours, ordered 2 ounces (59.2 cc.) of infusion of senna; 2 drachms (7.5 Gm.) of Rochelle salts; 4 grains (0.6 Gm.) of jalap and 1 grain (0.065 Gm.) of mild mercuric chloride, besides several "purging

1. The doses seemed so fantastic that the United States Bureau of Weights and Standards was consulted to see if the English and American measures of that day were comparable to those of the present time. The director was inclined to believe that they were, although he lacked definite information.

clysters." The infant survived! Apparently, here is a new and successful, if somewhat radical, treatment for cerebral hemorrhage masquerading under the guise of constipation.

Credit is given to American physicians for the use of mild mercuric chloride in croup, but Hamilton admits that the doses were enormous. One girl, aged 7 years, took 133 grains (8.66 Gm.) of mild mercuric chloride within sixty odd hours and two days later "appeared as if she had never had a complaint." Dunglison admits the possibility of salivation of children from mild mercuric chloride, but has never seen it occur under the age of 2 years, and Clarke has seen it only three times under 3 years of age. This is all the more remarkable when one realizes that ¼ grain (0.016 Gm.) of mild mercuric chloride often was given three or four times a day throughout the course of almost all the febrile diseases. The only thing that saved the children from a toothless existence probably was the castor oil given every two or three days during the same period.

But the therapeutic gem is produced by Dunglison of London. Master B., of Bromley, aged 1 year, after two days of constipation was attacked with violent vomiting, fever and abdominal distention, notwithstanding a purging of a watery nature unmixed with feculent matters. Four grains (0.26 Gm.) of scammony and 2 (0.130 Gm.) of mild mercuric chloride were given every four hours with some infusion of senna and syrup of rhubarb. On the next day, the vomiting and watery purging had nearly ceased, so the scammony and other drugs were repeated. On the third day, no feces had appeared, so a cathartic clyster morning and evening was ordered together with 1 grain (0.065 Gm.) of mild mercuric chloride and 4 grains (0.26 Gm.) of jalap, four times a day, in place of the former mixture. On the fourth day, the results had been nil except for a little mucus produced by the clysters, so a new combination was tried four times a day—4 grains (0.26 Gm.) of scammony, 2 grains (0.13 Gm.) of jalap with a mixture of infusion of senna and tincture of jalap, and also the clysters.

By the fifth day, no feculent material had appeared, although all the medicines had been retained. The symptoms of pyrexia were somewhat augmented; the child felt great disinclination to be moved (which is fairly obvious), and the fulness of the belly was considerable. The dose for the day was 1 drachm (3.75) Gm.) of aloes dissolved in 1 ounce (30 cc.) of simple syrup, to be given in divided doses every two hours together with the jalap and scammony powders. On the sixth day, all of the syrup having been taken and retained, our little hero had the first feculent motion since the commencement of his illness. The fullness of the abdomen was somewhat diminished, but fever persisted. The aloes and powders, therefore, were carefully continued. On the

seventh day, after two copious evacuations, the fever began to fall, so for good measure ½ grain (0.0325 Gm.) of mild mercuric chloride was given four times a day with an aperient mixture (specifications not furnished), and the child gradually became convalescent.

Dunglison modestly admits that this is one of the most stubborn cases he has ever had. Apparently, he had not exhausted his armamentarium because in another place he states that when senna and mild mercuric chloride and the other remedies had failed and when even yellow soap suppositories or clysters of aloes were ineffective, a warm bath or the application of leeches occasioned copious evacuations.

They were stout youngsters in those days, and they took their bleedings and blisterings as well as their cathartics. In treating patients who had croup, for example, Syer withdrew enough blood to induce syncope, usually from 6 to 8 ounces (178 to 236 cc.), and followed this by three or four leeches on the trachea and a full-sized blister on the chest.

Dunglison did not limit his efforts to the cure of constipation, but advocates bleeding for diarrhea. He remonstrates with the practice of continental physicians of applying leeches to the anus and cannot see that any advantage can be derived from their application there—"which would not be equally obtained by abstraction of blood from any portion of the abdomen."

And woe betide the bed-wetter in those ancient days, less he suffer from cantharides internally to the point of slight strangury, or cantharides locally in the uretha, or blisters or plasters of Burgundy pitch on the sacrum. And even gentle Dr. Dewees cured hydrocele by pouring on it 2 quarts of cold water from a height.

In the midst of such unphysiologic practices, a few could see the dangers. Hamilton objects to indiscriminate bleeding even by leeches on the score that infants need blood and cannot always repair its loss. Courzons of Birmingham (quoted by Underwood) decries the use of mild mercuric chloride in cases of diarrhea and believes that many children have fallen a sacrifice to its improper administration, to which Underwood replies: "Of what medicine may not this be said?"

And yet Underwood himself remarks that "nature alone will oftimes effect wonders for infants if she be not officiously counteracted." His difficulty and that of countless others even to this day, lay in a proper definition of "officiousness."

Not all the authors of the times were devoid of therapeutic acumen. Bateman says:

> We possess no physical agent, not even blood-letting, by which the functions of the animal economy are controlled with so much certainty, safety and promptitude as by the application of cold water to the skin under the augmented heat of scarlatina or some other fever.

DIAGNOSIS IN ANCIENT TIMES

There is abundant proof of their optimism and perseverance in treatment. Possibly mistaken diagnosis played a part. If all cases of croup were grouped and treated as the same disease, the mortality of laryngeal diphtheria would be offset by recoveries in spasmodic laryngitis.

One of the most amusing misconceptions was that of Syer, who, as an apologia for writing his book, states that a new point of view may be desirable, "notwithstanding that the subject of infantile infirmity has been apparently exhausted by the investigations of various writers."

Most interesting are the accounts of diseases which apparently are rarely, if ever, seen today, for example, hypertrophy of the brain as described by Condie. He carefully distinguishes it from hydrocephalus. It is observed most frequently in children of lymphatic temperament or in those with rickets, and may originate at any time from birth to puberty. Children are often born with large heads; in others, the head rapidly increases in size soon after birth, and within a short period attains an enormous magnitude. The fontanel feels firm. If cranium and brain develop pari-passu, there may be no symptoms, but one is apt to find drowsiness and apathy, while apoplectic seizures have been noted. If enlargement of the brain begins after ossification of the skull is nearly completed, intense headache supervenes with vertigo, dulness often amounting to idiocy, debility and finally general paralysis. Death often results with convulsions or apoplexy. Many children survive to puberty.

At autopsy a general enlargement is found with flattening of the convolutions, pallor and increased density of the cortex, a diminished amount of blood in the vessels and little or no serum in the ventricles and between the membranes. Sometimes the hypertrophy is confined to one lobe or to the corpora striata or the optic thalamus. The cerebellum rarely is affected. In some cases, the vessels of the pia are engorged; in others, a slight amount of reddish serum is found at the base; in others, a clot of blood with rupture of the medullary fibers may be detected. In a few, there may be more or less extensive softening, but in all of these instances death will have been preceded by symptoms of cerebral disease in addition to those which belong to hypertrophy of the brain.

Apparently streptococcal and other severe bacterial infections assumed strange appearances.

In esophagitis, according to Billard, there is frequent vomiting immediately after feedings. The child refuses fluids but often swallows half solid aliments. Deglutition is painful and emaciation is rapid, but there is little or no fever. Almost invariably stomatitis precedes the attack. At autopsy, irregular black eschars are found, with intervals of bright red excoriations and gelatinous softening of nearly the entire

thickness of the esophagus. The stomach may be involved but usually is normal! Darwell believes that this disease probably is the cause in many cases of obstinate vomiting!

Underwood describes malignant coryza in the new-born infant. This begins in the first or second week of life as a profuse purulent discharge; afterward it becomes sanious, and lasts several weeks. Death often occurs in convulsions. At one autopsy, nothing was found except extreme redness and turgor of the nasal mucosa.

A disease called skin-bound is described by most of the authors. This occurs in early infancy and chiefly in hospital practice; its outstanding characteristics are prostration, induration and swelling of the subcutaneous tissues over most of the body and limbs and a high mortality. It is evident from the descriptions that the authors included under one heading true sclerema neonatorum and some form of acute fulminating bacteremia. For example, in a few infants the skin is pale and the panniculus is waxy. In a majority, the skin is red or purple and autopsy shows effusion of yellowish or greenish sero-albuminous fluid into the subcutaneous tissues and between the muscles with an accumulation of black blood in all the viscera. The clinical resemblance of the latter type to erysipelas is noted by Eberle, Condie and others.

Some familiar diseases were more severe at that time than now. Robertson finds that the pulsation of the brain in rachitic children can be felt through the anterior fontanel as late as the fourth year, and all the descriptions allude to permanent crippling in some severe cases of rickets.

Dewees allows six weeks for whooping-cough to develop and six weeks for it to defervesce with a variable period for its height. It is rarely as bad as that today, with or without treatment. Hemorrhage from the nose and lungs was not unusual in pertussis, and Eberle finds that it is nothing uncommon for convulsions to occur. In Sweden, from 1749 to 1764, there were 43,393 deaths from chin-cough, as it was called. No wonder it was designated as a formidable disease.

One finds little or no mention of many other conditions that are well known today, in spite of the fact that experience at autopsy was by no means wanting. Intracranial hemorrhage in the new-born infant is described by Billard but is not credited to childbirth, nor is any form of hemorrhagic disease of the new-born mentioned, except bleeding from the umbilicus. In spite of Beardsley's description of pyloric stenosis in 1788, it was not generally recognized. Projectile vomiting is noted by Dewees, but deaths in such cases evidently were not frequent. The term rheumatism is used by Condie and Gervino to describe pain in the muscles, but no one describes acute rheumatic fever. Since little attempt was made to make a physical diagnosis of conditions of the

chest, heart disease is scarcely considered, with the exception of the congenital variety. Condie found pericarditis at autopsy, but expresses the opinion that its discovery during life can be only a guess. Clarke found an instance of propericardium after death and states that the strong impulse of the heart had been noted but was considered of no importance. Billard apparently was the only author who attempted its recognition antemortem.

In only one instance is there considered to be any relationship between convulsions and rickets, in spite of the florid character of the latter. The extreme pallor of anemia and leukemia with enlargement of the spleen and liver are not described. Purulent otitis media occurred occasionally, but only rarely was it associated with mastoiditis, meningitis and abscess of the brain. Ulcerative stomatitis was common, but the destruction brought about by noma is mentioned only by Billard in spite of the frequency of pertussis and measles. Most infants with diphtheria must have died of toxemia, since no one mentions the sudden death which occurs during early convalescence.

While nephritis in adults was known, few practitioners of pediatrics had any conception of such a condition in childhood, and the chapters on urinary diseases concern only disordered vesical functions and lithiasis. Diabetes was recognized by the sweet taste of the urine.

One noteworthy fact is that the child of that period apparently had no qualms about eating, as anorexia is mentioned only in connection with definite disease. Robertson alludes to spoiled children who are pampered by being allowed any food to their liking until they lose their natural appetite and develop chronic indigestion. The modern product who is brought up under a liberal dietary regimen which he more or less fails to take advantage of, apparently had no counterpart in those days.

It seems possible that the modern apotheosis of the child has had something to do with the increasing difficulties in securing the child's obedience to rules. When youth was taught to be seen and not heard he must have been more amenable to discipline. To bear with the modern recalcitrant child is the price one pays for the privilege of watching the childish bud unfold to the completion of its development unhampered and unashamed.

Of all the omissions, the lack of records of temperature, pulse and respiration probably is the most striking.

The old literature abounds in curious misconceptions with here and there a shrewd guess at the true facts. Croup and laryngeal diphtheria are considered together. Some physicians recognize the difference in type; most of them congratulate themselves when suffocation is aborted by their treatment for croup.

Experience with convulsions was wide and varied, and Eberle takes his fling at the reformers by ascribing the increase in the number of cases of convulsions to the vicious systems of educating infants in "modern times" (1832).

It is small wonder that dentition was in the diagnostic foreground when Underwood, the nestor of his times, states that he has known children, after being reduced by purging and other complaints and after lying for as much as three months, scarcely fit to be moved, with continual fever, flushed cheeks, emaciated, with a large belly and incessant cough and almost without taking any nourishment, to recover in a few days as it were on rapidly cutting half a dozen teeth. Clarke finds that those children in whom there is profuse salivation during dentition suffer the fewest inconveniences from the process.

Curious is the importance attached to the too sudden healing of eruptions on the skin, especially those behind the ears: "Unless the diet be lowered and the bowels kept open, the cure of skin ailments may be followed by organic affections of the brain."

In view of present day difficulties, one cannot afford to be hypercritical at the attempts made to classify the cases of diarrhea in ancient times. Apparently the method had the virtue of simplicity. If an infant with acute diarrhea died, the condition was either cholera infantum or dysentery, depending on the general consistency of the stools. When the mucus changes from white to pure pus, Dewees sees an analogy to the stages of a coryza and predicts therefrom the breaking up of the attack.

Nothing illustrates better the real poverty of the resources of the physicians of that age than Condie's statement that when pus forms in the chest (after pneumonia) the case is generally hopeless, although he had read of one patient who had been saved by operation!

From the description of remittent fever, it is evident that this term included typhoid fever, some cases of infectious diarrhea, probably pyelitis and endocarditis and certainly abdominal tuberculosis—to say nothing of typhus fever and possibly some cases of pneumonia.

On the other hand, a foreign body in the lung was well recognized even to the interruption to respiration in one lung when the corresponding bronchus was occluded, and tracheotomy, even at that date, had saved some patients. And yet, since this was before the general acceptance of Laennec's teaching, the diagnosis of pneumonia was made, not on the basis of physical signs, but on the occurrence of rapid breathing, cough and fever.

Under the heading hydrocephalus, all forms of meningitis, arachnitis and encephalitis besides the cases due to congenital defect and injury at birth were described. According to Eberle the mortality was practically 100 per cent, although Darwell naively credits himself with a

cure. A 10 month's old malnourished infant happened to be noticed one day in its nurse's lap, drowsy and languid, but without fever. The diet was changed from gruel to asses' milk, and 10 drops of aromatic spirits of ammonia were given every four hours. The next day the child was happy and laughing! Thus the alarmist has always reaped the reward which his better poised confrère misses.

Chorea, or chorea sancti viti as it was called, was better understood then than it is today, if one is to believe Hamilton, who claims that his father was the first to discover that it is "occasioned by irritation of the stomach and bowels." On this hypothesis, Parr of Exeter cured fifty-nine of sixty infants by the administration of repeated and powerful purgatives. Presumably the children were too weak to move. Condie mentions many forms of hysteria under the title chorea, although he recognizes the similarity between the two diseases. He describes salaam convulsions in choreic children, top-spinning and malleation (striking the knees with the hands); in one remarkable instance, the patient stood on his head and then fell over, repeating this as fast as he could for as long as fifteen hours consecutively. One would suspect that the good physician was letting him try for a record, since apparently no attempt was made to stop him. Condie further remarks that chorea at times continues with slight remissions, until the patient has reached an advanced age, and often persists until puberty. On the other hand, in emphasizing the importance of removing the cause of chorea before treatment can be successful, Condie specifies rheumatism among the etiologic factors.

Underwood describes an incident in which an infant was born when the mother was moving from her chair to the bed and, in consequence, fell with violence to the floor. The next day the infant became languid, recovering at intervals, but breathed faintly and died in stupor on the sixth day. The diagnosis was syncope, and probably many of the cases of injuries at birth in which death occurred were classified under this heading.

Intussusception was apparently not uncommon, and an early diagnosis was esteemed essential so that purgatives should be withheld. The only hope of cure lay in the sloughing of the intussuscipiens. Operation for intussusception was under consideration at this time (1824), but was believed by Dunglison to be inadvisable.

Malaria was well known and patients successfully treated with "the bark," as cinchona was designated. Underwood agrees with Sydenham that the ague-cake splenic enlargement is a favorable sign which indicates recovery.

Failure in diagnosis at times must have been due to poor observation and inadequate postmortem technic. Ayre describes a case of marasmus in a girl, aged 13 years, who had been coughing for six months and

who had dyspnea and pain in the chest, hectic fever and rapid pulse. Tarry stools developed, and finally a frank hemorrhage and death. Autopsy disclosed some old adhesions in the pleura, exsanguination of the viscera and nothing else!

Peritonitis, as described, must have been chiefly tuberculous. When properly treated in the first stages, according to Eberle, it can be readily subdued. When effusion is well marked, death is the ordinary result. He fails to make it perfectly clear how to recognize the first stages.

Purpura simplex was considered, if not identical with, at least analogous to, scurvy. The chief point in diagnosis, according to Evanson, is to discriminate from flea bites.

Rickets was once so prevalent in England as to be called by the Germans "die Englische krankheit." The prognosis in cases seen late was unfavorable, although marked improvement often took place at puberty. Many of the fatalities evidently were due to tuberculosis. Evanson remarks that these children sometimes show a remarkable fondness for salt. The causes of rickets were recognized as economic and hygienic, with heredity and prolonged suckling as factors.

Scarlet fever was well known, with its tendency to be followed by anasarca. Apparently hematuria was not noted, although albuminuria is mentioned by some authors. Few seem to have implicated the kidneys directly, although Condie notes the difference between the albuminous urine of scarlet fever and chronic interstitial nephritis and the similarity in the appearance of the kidneys at autopsy. He ascribes deaths in anasarca to "sudden effusion in the brain." Tweedie (quoted by Evanson) recognizes a scarlatina faucium, chiefly among adults, in which the typical rash occurs in the mouth but none on the skin; yet these cases are followed by desquamation.

One of the strangest facts related to the occurrence of thrush, a common disease evidently, which often eventuated in death from the ensuing diarrhea. The latter probably resulted from over medication internally, as the silver nitrate and borax used locally should have been fairly effective.

Condie's description of the scrofulous child is interesting. He claims that there is a "deficiency of fibrine in the blood with a predominance of white fluids and tissues over the red; the organs pale, small in size, loose in texture and perform languidly their respective functions. There is a peculiar fragility of the whole frame; the skin is usually thin and delicate; the limbs are small, soft and rounded but with large joints, the fingers are long and slender but often broad and flat at the extremities. The chest is contracted, the head usually large and the hair fine and silky, the eyelashes long, the eye prominent but languid in expression, the pupil large and the lips usually thick and prominent."

"The countenance is, however, not infrequently swollen and sallow in hue, the cheeks full, tumid and flaccid, the hair coarse and the skin harsh, the eyelids drooping." There is something in this that is strangely reminiscent of the pronouncement of some of the present day experts on status thymolymphaticus. From the ethereal angel type child to the thick-lipped, coarse, Ethiopian type is quite a step—when both are supposed to develop from the same cause.

In describing the stoppage of the nose in scrofulous children, Osiander (quoted by Von Mezler) advises that the children be taught the use of snuff.

Tetany, with its carpopedal spasm is recognized but not named and is ascribed to teething. Tetanus neonatorum was particularly prevalent on the island of Jamaica, and Underwood rejoices that James Clarke has at length clearly ascertained its cause, namely, the smoke from burning wood. The negro homes in Jamaica were constructed without chimneys, and it was found that in the houses without fires, tetanus did not occur.

Thymic asthma, laryngismus stridulous, inward fits, Millar's asthma and spasm of the glottis, were hopelessly confused. Even at that time, the fascination of thymic death had intrigued clinicians so that Evans and Mansell complain that this heterogeneous syndrome is being foisted on the thymus, and thus it is becoming the "asylum ignorantiae" in all cases of sudden and unaccountable death in young children. Condie doubts that the thymus is actually enlarged often, since it is not known what constitutes a normal size.

Syphilis is frequently transmitted by the nipple of a wet-nurse, according to Condie, but treatment by mercury begun at an early stage is, in his opinion, generally successful in from one to four months. He is careful to note, however, that there is a liability to recurrence.

Finally, one must consider the subject perhaps more fascinating to the ancient scribes than any other—worms. A few recognize their comparative rarity while willing to admit that severe symptoms may follow their presence. One, Gervino, carries his belief to such lengths as to ascribe most febrile diseases and many others, to the presence of heterogeneous substances in the bowel—particularly worms. Since dead worms can be digested, according to his belief, the mucus evacuated after drastic purgation is in reality the sloughs of dead worms and, reductio ad absurdum, he describes the cure of rickets in a 13 months old infant by the administration of an anthelmintic to her wet-nurse.

A quotation from Dewees, anent Good's advice for brisk purgation in the treatment of worms, is a delightful sample of a courteous denial of another's point of view.

> We confess ourselves to have high respect for the learnings and talents of this gentleman (Dr. Good) but for many years it has been our deliberate opinion that

it (purgation) may prove mischievous by making these animals cling more closely to the bowel and thus disappoint the expectations of the practitioner. We therefore never prescribe a purgative when about to assail these animals.

COMMENT

In summing up the experience of the past, one finds that then, as now, the greatest morbidity and mortality occurred among the poor and ignorant from infections and malnutrition. The greatest achievements have been made in combating these evils.

The greatest fault of the ancients probably lay in their too great faith in drugs and bleeding. They can hardly be blamed for their ignorance of physiology, and lest the modern attitude toward their heroic treatments become too hypercritical, it is well to remember that some of the serum and intravenous therapy used today may seem equally uncouth to our descendants 100 years from now.

One should never cease to admire and to emulate their courage, their patience and their optimism in the face of ghastly odds. Taking them all in all, they probably exhibited about the same proportion of skill and stupidity, of judgment and of error, of poise and of instability as we see today.

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METABOLISM OF TOTAL BASE IN NEPHRITIS*

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The results of studies on the salts of the blood and excreta in nephritis were reported in previous papers.[1] The observations in this paper were made of the total base as found in these cases and on some further estimations on the total base in the blood by a modification of Fiske's method.

The results obtained in the study of the total base of the plasma are given in table 1. The relatively slight variation in the concentration of total base of the plasma in different types of nephritis and under varying conditions is apparent. Marked abnormality is noted in only two serums. Others, however, are at the lower limits of normal and are lower than those found by Blackfan and Hamilton[2] in nine children who were nearly normal, namely, from 156 to 161 cc. tenth-normal base per hundred cubic centimeters of blood. Possibly some of our figures are a little too high, as values of the total base determined by estimation of the separate elements tend to be a little higher than do those obtained by Fiske's method.[3] For example, Kramer and Tisdall[4] gave from 156 to 159 cc. tenth-normal base per hundred cubic centimeters of plasma as normal according to determinations of separate elements, whereas from 147 to 161 (Peters et al.[5]) or from 136 to 163 cc. tenth-normal (Briggs[6]) are the normal values obtained by others determining the total base by direct methods.

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* Received for publication, March 8, 1928.

* From the Laboratories of the Sub-Department of Pediatrics, University of Toronto and of the Hospital for Sick Children, and from the wards of the Hospital for Sick Children.

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Too few cases of any one type of nephritis were studied to justify the conclusion that certain deviations from normal, or their lack, characterize any specific renal lesion. The only consistent variation noted was the diminution of the total base concentration in all cases of the chronic diffuse or interstitial variety. Bulger,[7] Peters and others previously reported the decrease in the total base as characteristic of this type of nephritis, and they regarded it as at least partially responsible for acidosis.

Tendencies toward high or low bases of the plasma are not associated with similar variations in the excretion of these substances, except in the

TABLE 1.—*Bases of Blood in Terms of Tenth-Normal*

Case	Sodium	Potassium	Calcium	Magnesium	Total Base	Protein, per Cent	Corpuscles, per Cent	Nonprotein Nitrogen, Mg.	Creatinine per 100 Cc.	Phosphates per 100 Cc.	Edema	Acidosis or Uremia	Diagnosis
R. B.	148	4.8	4.7	1.6	158.5	....	25	..	1.4	5.0	0	0	Acute glomerulonephritis
Al. J.	148	5.3	4.0	1.4	158.7	....	50	..	1.2	5.0	0	0	Acute glomerulonephritis
A. J.	141	4.7	4.6	1.5	151.8	6.0	50	30	...	5.5	0	0	Acute tubular nephritis
A. C.	156	5.0	4.7	1.4	167.1	6.10	50	..	1.3	3.8	++	0	Acute tubular nephritis
C. B.	...	....	...	...	155	6.12	41	35	1.5	...	++	+	Acute tubular nephritis
D. H.	154	5.2	5.0	1.4	165.6	....	50	..	1.5	5.0	+++	0	Acute tubular nephritis
B. R.	...	...	...	...	142.5	4.10	30	65	1.9	4.8	++++	0	Syphilitic nephritis
N. W.	143	5.0	4.0	1.5	153.5	....	52	..	1.4	5.8	Slight	0	Acute mixed nephritis
R. K.	...	...	...	...	160.0	6.77	47	40	1.25	4.6	+	0	Acute mixed nephritis
G. B.	141	5.3	4.4	1.4	152.6	....	25	..	2.0	7.0	+	++	Acute mixed nephritis
B. C.	144	4.9	4.5	1.5	154.9	....	44	45	1.4	7.0	+++	+	Acute mixed nephritis
W. H.	145	5.2	5.0	1.6	154.8	....	46	60	...	7.5	0	0	Acute mixed nephritis
G. C.	150	5.1	4.9	1.5	161.6	6.5	50	..	1.5	3.0	0	0	Acute mixed nephritis
E. D. 1	152	5.5	3.6	1.2	162.3	5.0	41	..	1.8	6.3	++++	0	Chronic tubular nephritis
E. D. 2	147	5.3	4.4	1.4	158.1	5.0	35	60	2.0	6.0	+	0	Chronic tubular nephritis
O. C.	...	...	...	...	150	7.20	26	30	5.0	9.0	++++	+	Chronic tubular nephritis
I. T. 1	141	5.1	4.5	1.5	152.1	6.55	35	..	6.5	6.5	+	+	Chronic interstitial nephritis
I. T. 2	...	...	...	...	148	6.92	36	..	2.5	8.0	Slight	+	Chronic interstitial nephritis
A. T.	...	...	...	...	149	....	..	..	...	9.6	Slight	+	Chronic interstitial nephritis
G. A.	141	4.7	4.7	1.5	151.1	....	60	..	2.0	8.0	+++	+	Cardiorenal

case of sodium chloride. All the patients with a positive balance of sodium chloride showed a tendency toward decreased concentration of the total base of the plasma. This is more particularly so in those in whom this retention of salt is associated with edema; E.D. 1 was the only exception. For some inexplicable reason, she had a sufficient increase in the blood sodium to increase her total base.

The total base of the plasma was constantly diminished in all cases in which there was clinical acidosis and in all the patients whose blood phosphates were in excess of 5 mg. per hundred cubic centimeters of

7. Bulger, H. A.; Peters, J. P., Eisenman, A. J., and Lee, C.: J. Clin. Investigation **2**:213, 1925-1926.

blood. Only one patient with an abnormally low blood base did not show clinical evidence of acidosis and did not have retention of phosphate as indicated by a blood phosphate. This patient was dying of syphilitic nephritis and had marked general anasarca and edema when the observation was made. The low base, as already pointed out, may be the cause of the nephritic acidosis, and the retention of phosphate in the blood may play a secondary rôle.

The relation between blood dilution and base concentration is not clear. Van Slyke, Wu and McLean [8] have pointed out that the base of the plasma varies somewhat with the migration of water in and out of the corpuscles. In this series, a constant relationship could not be demonstrated between the cell volume and the total base of the plasma. Neither could a constant variation of base content and blood dilution

TABLE 2.—*Urinary Excretion or Base in Terms of cc. Tenth-Normal*

Case	Age	Sodium	Potassium	Calcium	Magnesium	Total	Cc. Base per 100 Cc. Urine	Edema	Diuresis	Acidosis	Diagnosis
R. B.	6	123.2	330	13.3	20.3	486.8	60	0	0	0	Acute glomerulonephritis
Al. J.	13	739	517	12.2	55.2	1,323.5	89	0	0	0	Acute glomerulonephritis
A. J.	5	322	553	11.7	35.0	921.7	72	0	0	0	Acute tubular nephritis
A. C.	13	707	461	13.4	39.0	1,220.4	80	++	+	0	Acute tubular nephritis
N. W.	10	579	414	22.0	11.0	1,026	81	Slight	+	0	Acute mixed nephritis
G. B.	11	60	156	12.3	18.0	246.4	55	+	0	++	Acute mixed nephritis
B. C.	11	466	437	18.0	13.6	934.6	80	+++	0	+	Acute mixed nephritis
W. H.	8	388	544	13.0	62.7	1,007	55	0	+	0	Acute mixed nephritis
G. C.	10	445	335	14.2	30.6	814.8	102	0	0	0	Acute mixed nephritis
E. D. 1	6	...	...	....	....	.....	..	++++	0	0	Chronic tubular nephritis
E. D. 2	7½	171	403	15.0	34.9	623.9	73	+	0	0	Chronic tubular nephritis
I. T.	8	84.3	433	15.8	24.6	561.7	59	+	0	+	Chronic interstitial nephritis
G. A.	8	191	466	13.8	40.3	711.1	130	+++	0	++	Cardiorenal

be demonstrated when the degree of the latter was judged by the serum protein. Low blood protein was frequently associated with low base, but not in all cases.

The presence or absence of edema did not exert any influence on the level of the base of the plasma except in the cases previously mentioned in which edema and retention of sodium chloride were coexistent.

Retention of nitrogen or its absence, as indicated by blood nonprotein nitrogen or creatinine values, exerted little effect on the level of the base of the plasma. In fact, in the two types of nephritis most commonly associated with a low base, one, the acute tubular, is characterized by a lack of retention of nitrogen, while the other, chronic interstitial, usually shows its presence to a greater or less extent.

In the study of the excretion and general metabolism of total base, we have made use of the figures obtained by Sawyer,[9] Baumann and

8. Van Slyke, D.; Wu, H., and McLean, F. C.: J. Biol. Chem. **56**:765, 1923.
9. Sawyer, M.; Baumann, L., and Stevens, F.: J. Biol. Chem. **33**:103, 1918.

Stevens in their study of these substances in normal children. These authors investigated the base and acid metabolism of two normal children, aged 5 and 8 years, on normal and on high fat diets. Their base intake was comparable to that in our pathologic cases, the chief difference being in the relative proportions of calcium and sodium. These observations were more complete than most of those available, in that fecal as well as urinary excretion was studied. The normal figures referred to in this study are those of these authors plus a few unpublished figures obtained by one of us (A.M.C.).

As previously shown,[10] the nephritic kidney is unable to excrete sodium in normal concentration unless the damage is so mild as not to cause any functional impairment of the kidney or in the more severe cases, when diuresis is present. The decreased excretion of sodium by the kidney is present whether there is edema or not, but is more marked in hydræmic cases. Only two of our patients could concentrate the urinary sodium to normal: one had so mild a lesion that the kidney acted as normal, and the other child was examined during the excretion of the edema.

The results of a study on the decreased urinary excretion of calcium[11] and magnesium[3] have also been reported previously. Despite a considerably larger calcium intake, the urinary excretion of calcium of patients with nephritis was only about one-tenth that of normal persons. Renal acidosis, unlike that produced by a diet rich in fat, did not exert any effect on the calcium in the urine. The lower renal excretion of magnesium salts is most evident in edema, when only about 25 per cent of that of normal persons is excreted.

Potassium, as previously shown,[3] apparently does not offer any difficulty of excretion to the nephritic kidney. In most cases the urine of the patients with nephritis contained even more potassium than did that of normal persons. Acidosis produced by diets rich in fat apparently increases the excretion of these salts, but nephritic acidosis was ineffectual in this respect.

The amount of fixed base excreted by the diseased kidney appears to depend largely on the ability of the latter to excrete its constituent elements. In only four patients with nephritis did the urinary excretion of fixed base approach normal. Diuresis, except in a severe nephropathy, causes an increased excretion by the kidney. In severe cases, diuresis plus a generous intake was powerless to raise the urinary secretion of fixed base to a normal level.

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10. Boyd, G. L.; Courtney, A. M., and MacLachlan, I. (footnote 1, third reference).

11. Boyd, G. L.; Courtney, A. M., and MacLachlan, I. (footnote 1, first reference).

Few observers have considered fecal excretion capable of playing any important rôle in the maintenance of the acid-base equilibrium of the body. Studies by Stohl and Sato [12] and by Goldschmidt and Dayton [13] show that the bowel normally participates in the neutrality regulation of the body by excreting alkali. If such a function is served normally by the bowel, one might expect that in the case of the overburdened nephritic kidney, unable to excrete in a normal manner, increased fecal excretion might serve to prevent an abnormal retention of base in the body. That such increased excretion of base by the bowel can take place in the presence of inadequate urinary excretion is demonstrable in our cases. The proportion and amounts of potassium excreted by the bowel were unaltered, this being the one base apparently readily handled by the nephritic kidney. Sodium, calcium and mag-

TABLE 3.—*Fecal and Total Excretion of Base Intake and Retention in Terms of Tenth-Normal*

Case	Sodium	Potassium	Calcium	Magnesium	Total	Total Excreted	Total Intake	Retention
R. B.	23.6	49.4	460.5	73.6	607.1	1,093.9	1,159.3	+65.4
Al. J.	30.6	57.5	491.2	66.2	645.8	1,969.3	1,175.0	—794.3
A. J.	51.0	52.0	771.0	95.0	969.0	1,889.7	1,325.3	—564.4
A. C.	144.0	106.7	686.6	123.9	1,061.2	2,281.6	959.4	—1,322.3
N. W.	30.2	89.0	789.4	120.0	1,028.6	2,054.6	1,409.3	—645.3
G. B.	8.4	11.4	506.4	480.0	1,006.2	1,252.6	338.5	—914.1
B. C.	157.0	114.8	987.7	142.1	1,401.5	2,336.1	1,653.1	—683.0
W. H.	45.8	49.6	554.4	89.0	738.8	1,946.5	1,398.8	—347.7
G. C.	69.0	93.7	761.0	54.6	978.3	1,793.1	1,186.0	—607.1
				Urine and Feces				
E. D. 1.	70.0	424.8	576.8	148.0	1,218.5	1,218.5	1,138.2	—80.5
E. D. 2.	31.3	49.3	578.5	87.0	745.3	1,369.2	1,359.5	—10.0
I. T.	39.0	71.2	829.4	124.6	1,064.2	1,625.9	2,456.3	+830.4
G. A.	25.9	61.4	723.8	104.0	915.1	1,626.2	1,266.8	—359.4

nesium, which the kidney was incapable of excreting efficiently, were all proportionately and actually increased in the feces. For example, normally from 0.58 to 1.6 per cent of the sodium intake was found in the feces, whereas in cases of nephritis, from 5 to 20 per cent of the intake was excreted by the bowel. The increase in the fecal magnesium is great enough, not only to overcome the effect of its diminished concentration in the urine, but to produce the negative magnesium balance frequently found in nephritis. The calcium intake in the pathologic cases was greater than in the normal, but the increment in the calcium content of the feces in patients with nephritis was greater than could be accounted for by this alone.

The total base of the feces is higher in those patients who had, or who had previously had, edema. In hydremic cases, the total base of the feces ranged from 915 to 1,400 cc. of tenth-normal base per day:

12. Stohl, A. T., and Sato, A.: J. Biol. Chem. **58**:235, 1923-1924.
13. Goldschmidt and Dayton: Am. J. Physiol. **48**:473, 1919-1920.

whereas in nonedematous patients, figures from 607 to 978 cc. of tenth-normal base per day were obtained. The larger excretion in dropsical cases was due to increased loss through the bowel of all basic elements except potassium. Renal acidosis was accompanied by increased fecal base in excess of that produced by induced acidosis in children fed on diets rich in fat.

The total base excretion, urine and fecal, in patients with nephritis exceeded that in normal children, despite a comparable intake. It is significant that in patients with nephritis a much larger proportion of the base is excreted by bowel than in normal persons. This is most striking in severe cases in which impairment of renal function prohibited adequate excretion of these salts in the urine.

Edema exerts considerable influence on the amount of base excreted. In the first place, the actual excretion is greater, and, in the second, a larger proportion is excreted in the feces, 54 per cent as apposed to 44 per cent in nonedematous cases.

SUMMARY

1. The concentration of the base of the plasma in nephritis swings in both directions, but distinct variations from normal are infrequent.

2. A decrease in the concentration of the base of the plasma to a low normal level or to a level lower than normal is constantly found when the following conditions are present: (*a*) renal acidosis with increase in the blood phosphate; (*b*) the end state of a chronic interstitial nephritis, and (*c*) a positive retention of sodium and chlorine in the body, particularly when this is associated with edema.

3. A constant relationship could not be demonstrated between the base of the plasma and the following: (*a*) retention of nitrogen as indicated by blood nonprotein nitrogen or creatinine; (*b*) blood dilution, whether gaged by the cell volume or by the protein content of the serum, and (*c*) base retention by the body other than sodium retention.

4. The excretion of total base by the nephritic kidney is usually less than normal unless the lesion is so mild that functional impairment is not present or unless diuresis is occurring.

5. Fecal excretion of total base and of most of its constituent elements is increased in patients with nephritis whose kidneys are incapable of excreting normal amounts of fixed base. This increase in the proportion of base excreted by the bowel is most noticeable in edematous cases.

6. Nephritic patients frequently excrete larger amounts of fixed base than do normal persons.

AURICULAR FIBRILLATION IN CHILDREN

ITS RELATION TO RHEUMATIC HEART DISEASE*

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Incidence
Clinical Classification
Paroxysmal Auricular Fibrillation
Terminal Auricular Fibrillation
Chronic Auricular Fibrillation
Comment
(a) Extrinsic Factors and the Development of Auricular Fibrillation
(b) Acute Rheumatic Fever and the Development of Auricular Fibrillation
(c) Mitral Stenosis and the Development of Auricular Fibrillation
(d) Digitalis and the Development of Auricular Fibrillation
Differential Diagnosis
Treatment
Prognosis
Conclusions

Auricular fibrillation has been considered an unusual and infrequent type of irregularity in children during the course of rheumatic fever.[1] Modern texts in pediatrics fail to mention its relative importance in the acute phase of the disease or its occurrence as a complication of long standing cardiac involvement.[2] A summary of the literature since the introduction of the electrocardiograph seems to confirm this belief concerning the apparent rarity of this irregularity in children with rheumatic

* Received for publication, Feb. 7, 1928.

* From the Service of Dr. B. S. Oppenheimer, the Medical Division of the Montefiore Hospital for Chronic Diseases, New York. Read before the Section of Pediatrics, New York Academy of Medicine, Dec. 8, 1927.

1. Hecht, A. F.: Der Mechanismus der Herzaktion im Kindesalter, seine Physiologie und Pathologie, Ergebn. d. inn. Med. u. Kinderh. **11**:324, 1913. McCulloch, H., and Rupe, W. A.: Tolerance of Children for Digitalis, South. M. J. **15**:381, 1922. Sutherland, G. A.: Some Forms of Cardiac Irregularity in Children, Clin. J. **51**:181, 1922. Coombs, C. F.: Rheumatic Heart Disease, New York, William Wood & Company, 1924, pp. 216-225. Vaquez, H., and Donzelot, E.: Les troubles du rhythme cardiaque, Paris, Bailliere & Fils, 1926, p. 130.

2. Bass, M. H.: Chapter on Acquired Diseases of Heart, in Abt: Pediatrics, Philadelphia, W. B. Saunders Company, 1924, pp. 389-391. Nobecourt, P.: Clinique medicale des enfants; Affections de l'appareil circulatoire, Libraires de l'Academie de Médicine, Paris, 1925, p. 244. Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, ed. 9, New York, D. Appleton & Company, 1926, pp. 482-485.

heart disease.[3] Only nine of the thirteen cases reported in children under the age of 11 with auricular fibrillation give a definite history of an antecedent or concomitant rheumatic manifestation.[4] Authentic figures of this arrhythmia in children up to the age of 15 are wanting.

During a recent study of children who have been under observation at the Montefiore Hospital over a prolonged period of time,[5] we were so impressed with the frequency of both the transient and the permanent form of auricular fibrillation in rheumatic fever, that we have attempted a systematic search to determine its prevalence and to discover its influence and bearing on heart failure. We tried in particular to learn what factors besides the involvement of the heart muscle itself were responsible for the initiation of the arrhythmia. In this connection repeated electrocardiograms have been of invaluable aid.

INCIDENCE

Between the fall of 1921 and the spring of 1927, there were admitted to our wards sixty children between the ages of 5 and 15 with chronic rheumatic cardiac valvular disease. All had definite histories of recurrences and exacerbations of the disease prior to the admission, and in every instance there was advanced organic involvement of the heart. Ten of the sixty children showed auricular fibrillation at some time during their stay in the hospital. There were five boys and five girls. These children represent 4.2 per cent of 233 cases showing fibrillation of the auricles from all causes that were admitted to the institution dur-

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3. Resnick, W., and Scott, G.: Auricular Fibrillation: Report of a Case in a Child Aged Four Years, Am. J. Dis. Child. **31**:357 (March) 1926.

4. Coombs (footnote 1, fourth reference). Nadel, V.: Ein Fall von Flimmerarhythmie in Kindesalter Mitt. d. Gesselsch. f. inn. Med. u. Kinderh. in Wien. **12**: 210, 1913. Ehrenreich, S. G.: Case of Auricular Fibrillation in a Child, New York M. J. **99**:269, 1914. Neuhof, S.: Clinical Cardiology, New York, The Macmillan Company, 1917, p. 63; Auricular Fibrillation, M. Clin. N. Amer., 1920, p. 323. Ogden, R. T.: Auricular Fibrillation: Report of a Case in a Child Aged Ten Years, Am. J. Dis. Child. **27**:767 (June) 1925. Nobecourt, P., and Pichon, E.: Rhumatimse cardiaque evolutif avec insuffisance auriculaire gauche chez une fille de dix ans, Arch. d. méd. d. enf. **28**:493, 1925. Samet, B., and Tezner, O.: Ueber Digitaliswirkung bei gesunden und kranken Kindern ohne Herzinsuffizienz, Monatschr. f. Kinderh. **31**:301, 1926. Sidel, N., and Dorwart, F. G.: Quinidine Sulphate in Auricular Fibrillation, Boston M. & S. J. **196**:216, 1927. Sutherland, G. A., and Coombs, C. F.: A Case of Acute Rheumatic Carditis and Auricular Fibrillation in a Child, Heart **5**:15, 1913-1914. (The child cited by Sutherland and Coombs did not show auricular fibrillation as quoted by them but only premature beats as is indicated in the radial tracing accompanying their protocol. For this reason we are not including it here.)

5. Boas, E. P., and Schwartz, S. P.: Some Modes of Infection in Rheumatic Fever, Am. Heart J. **2**:375, 1927.

ing the same period (table 1). In six children the onset of the arrhythmia was noted during the acute phase of the rheumatic infection when the temperature was above the normal.

For purposes of clinical classification we have divided these cases into three groups: (*a*) the paroxysmal type, in which the arrhythmia was noted as a transient phenomenon and in which restoration of normal sinus rhythm took place spontaneously without the influence of drugs such as atropine or quinidine (in one of these cases, not considered in this paper, transient periods of auricular fibrillation were noted in a child following the administration of digitalis during auricular flutter before the establishment of normal rhythm); (*b*) the terminal type of only a few days' duration, usually noted as a fatal complication at the height of an acute exacerbation of rheumatic fever, and (*c*) the chronic or permanent form commonly associated with long-standing rheumatic valvular heart disease with or without hyperpyrexia.[6]

TABLE 1.—*Age Incidence in Auricular Fibrillation*

	0-10 Years	11-15 Years	16-20 Years	21-30 Years	31-40 Years	41-50 Years	51-60 Years	61-70 Years	71-80 Years	81-90 Years	91-100 Years
Montefiore Hospital—233 cases	4	6	9	10	34	36	61	45	19	8	1
Lea—69 cases	0	0	3	5	17	19	13	8	4	.	.
Semerau—111 cases	0	1	1	6	24	26	18	24	10	1	.
Coombs *—58 cases	2		2	8	14	17	11	4	..	.	.
Mackenzie—500 cases	.	(under 20 yrs.) 5		19	55	85	143	128	54	11	.

* Rheumatic heart disease, only.

PAROXYSMAL AURICULAR FIBRILLATION

Paroxysmal auricular fibrillation was studied and recorded in one child. The auricular irregularity appeared simultaneously with a bigeminal rhythm due to alternate premature ventricular beats. The fibrillation was of six days' duration and ceased one day before the premature ventricular beats disappeared. Two days before the boy's death there was complete restoration of normal sinus rhythm. Both types of arrhythmia came on at a time when the boy was thought to be recovering from an exacerbation of rheumatic fever that appeared one month before death. The temperature at that time was only slightly above the normal level; he showed signs of cardiac failure, such as moist râles at both bases posteriorly, and an enlarged liver.

6. Since this paper was written there were eleven additional children admitted to the wards, four of whom showed auricular fibrillation. One was of the terminal type and three of the permanent form. This makes a total of fourteen children with auricular fibrillation seen in seventy-one admissions to the hospital.

The following is a report of the case. The unusual complication of alternate premature beats will be discussed later.

CASE 1.—*Chronic rheumatic cardiac valvular disease; mitral stenosis and insufficiency, aortic insufficiency, transient auricular fibrillation, premature ventricular beats, bigeminal rhythm.*

A. B., a boy, aged 13, was admitted to the hospital complaining of precordial pain, dyspnea on exertion and cough. The symptoms had become progressive in the year previous to admission. Repeated sore throats necessitated a tonsillectomy at the age of 10. At that time he began to exhibit choreiform movements which persisted for six weeks. He had one severe attack of rheumatic fever before he was admitted to the Montefiore Hospital with signs of a recent exacerbation, accompanied by large erythematous patches over both his knees. These persisted for several weeks; his temperature remained elevated, he showed signs of congestion of the lungs, and his liver became enlarged to 9.5 cm. below the costal margin. His pulse rate ranged between 100 and 120 beats per minute and his blood pressure was 110 systolic and 60 diastolic.

With rest in bed, he improved and remained free from fever for the ensuing ten weeks, when, during an epidemic of rheumatic fever in the ward (November, 1926), he had a recurrence that was followed two months later by progressive signs of decompensation. At this time, he showed edema of the lower extremities, back and scrotum. He was digitalized, the initial dosage being 2 cc. of the tincture twice a day. Under this form of therapy his weight dropped within a month from 100 to 81 pounds (45.4 to 36.7 Kg.). His liver remained enlarged, however, so that the administration of digitalis was continued in daily doses of 1 cc. of the tincture. Despite the continued use of the drug, the boy became progressively worse and again developed signs of fluid retention with marked anasarca. During all this time, his temperature was only slightly above the normal. One month before death, he began to show signs of an active carditis and the temperature became elevated to 103 F. A more moderate fever persisted until the onset of an attack of paroxysmal auricular fibrillation which was noted clinically eight days before his death. At this time the rate at the apex was 96 and the rhythm was totally irregular, while the rate at the wrist was 68, and the beats varied in strength. An electrocardiogram revealed, in addition to the auricular fibrillation, a bigeminal rhythm due to alternate premature ventricular beats.

While the transient arrhythmia appeared insidiously unaccompanied by premonitory symptoms such as nausea and vomiting, nevertheless, during its presence, the boy began to show severe signs of heart failure. He became intensely cyanotic; breathing was labored, and his body was moist, cold and clammy. His hands and feet became swollen, and in spite of the continued use of digitalis in doses of 1.5 cc. per day, there was no improvement.

Three days before his death, the auricular fibrillation disappeared and the heart rate became more regular, averaging about 104 beats per minute, being interrupted only occasionally by premature beats. These finally vanished so that his heart rate and rhythm were perfectly regular for two days before his death.

TERMINAL AURICULAR FIBRILLATION

Terminal auricular fibrillation is so named because it is noted as a complication of rheumatic fever only shortly before death and sinus rhythm is not reestablished. We have observed three children who belonged to this group. The auricular fibrillation set in during active

carditis with hyperpyrexia. In two cases, with the onset of the irregularity the temperature fell to a subnormal level and persisted till death. In one case complicated by bronchopneumonia, the temperature remained elevated till the end.

The onset of the arrhythmia is sudden, with few, if any premonitory signs. Cyanosis is intense, dyspnea is marked, the respirations are labored and grunting, the sensorium is disturbed and the heart's action becomes totally irregular and uncontrollable. The picture presented is one of a severe form of heart failure that runs its course for only a few days and ends in death. Medication is of no avail.

The following three cases illustrate the syndrome of terminal auricular fibrillation in children.

CASE 2.—*Chronic rheumatic cardiac valvular disease; mitral stenosis and insufficiency, aortic insufficiency, sinus arrhythmia, bradycardia, partial heart block, terminal auricular fibrillation.*

A. J., a boy, aged 7½, who had chorea at the age of 3, had his first attack of rheumatic fever at the age of 4. During the following three years, he had several exacerbations of the disease, so that he was bedridden most of the time. At the age of 7, he began to show signs of decompensation, for which he was treated at a hospital. Six months later he was transferred to our ward, where it was noted that his heart rhythm was regular. In the spring and fall of his eighth year, while at our hospital, he had two severe recurrences of rheumatic fever, the latter ending fatally.

The onset of his last attack of fever was ushered in by a partial heart block with many dropped beats alternating with a marked sinus bradycardia. The pulse rate would drop suddenly to 40 a minute, and increase just as suddenly to over 120 beats a minute. These sudden variations in pulse rate were accentuated by deep respirations. The blood cultures were sterile. One month later, although the infection had somewhat subsided, his pulse rate remained at about 120 beats a minute. Digitalization was then begun in the usual manner, the patient being given 2 cc. of the tincture twice a day. This dose was continued for one month until six days before his death, when he refused all medication. Four nights before his death, the night before he collapsed and became unconscious, he had been restless and had complained of severe precordial pains. The fever persisted, the heart failure became more severe, and the boy became progressively worse until he collapsed and became unconscious.

On the morning of the following day, the temperature dropped to a subnormal level and remained so until death, which occurred three days after the onset of the auricular fibrillation. When seen on the morning after his collapse, he was intensely cyanotic, his respirations were 46 a minute and labored, and the temperature was elevated. The superficial veins of his neck were engorged, their pulsation was irregular and showed the ventricular form of venous pulse. The heart rate was totally irregular, and there was a pulse deficit of 20 beats a minute. The lungs were clear, except for a few sibilant râles at the bases posteriorly. This arrhythmia persisted till the end.

CASE 3.—*Chronic rheumatic cardiac valvular disease; mitral stenosis and insufficiency, aortic insufficiency, terminal auricular fibrillation.*

D. N., a boy, aged 10, was first seen in the cardiac clinic of the hospital one year prior to admission to the ward. At that time, he gave a history of "heart

trouble" of one year's duration. Because of dyspnea on walking, he was sent to a convalescent home, but he soon became ill and had to be transferred to the hospital. Three weeks prior to admission he began to cough and he complained of pain in the left side of the chest and expectorated green but not blood-tinged mucus. On the day before admission, he had a definite chill with elevation of temperature to 105 F., the pulse was 130 per minute and the respirations were 60.

On admission, he was delirious, intensely cyanotic and showed signs of bronchopneumonia at the lower base of the right lung. His heart rhythm, however, was regular. There were no signs of decompensation, his liver was palpable, and there was no edema of the legs. On the following day, the lower lobe of the left lung also became involved, and six days after admission he developed a pericardial friction rub.

On the eighth day in the hospital, the heart rhythm became absolutely irregular, his temperature was 103 F., the respirations were 50, the pulse was 102 a minute, and there was also severe diarrhea. With the onset of the arrhythmia, he became irritable, restless, intensely cyanotic and markedly dyspneic. The boy became progressively worse, and on the eleventh day he died suddenly while attempting to get out of bed. No other cardiac irregularities were noted throughout the period of observation. In his case, the high temperature persisted until death. During his stay in the hospital, he received one tablet of a digitalis preparation three times a day.

CASE 4.—*Chronic rheumatic cardiac valvular disease; mitral stenosis and insufficiency, aortic insufficiency, sinus bradycardia, premature ventricular beats, terminal auricular fibrillation.*

M. B., a boy, aged 10½, was first known to have heart trouble at the age of 7. Between that time and his admission to the Montefiore Hospital, he had been at another institution on three different occasions for recurrences of rheumatic fever. The last two attacks were accompanied by general anasarca. In the first five and a half months' stay at our hospital, he remained practically free from fever and symptoms of cardiac embarrassment. Two and a half months prior to his death, he developed signs of active pericarditis, erythema, petechial spots, progressive anemia and high fever, but no signs of heart failure. Fifteen days before the onset of auricular fibrillation at a time when he was not receiving digitalis, there was observed a definite slow pulse rate of 46 beats per minute with premature beats.

Four days before death, the boy became acutely ill. His respirations were rapid, shallow, and accompanied by a respiratory grunt. Petechial spots were noted on his hard and soft palate. In a limited area at the base of the left lung adjacent to the spine there was dulness, bronchial breathing and increased whisper, but no râles. The pulmonary signs were attributed to atelectasis of the left lung as a result of pressure by an enlarged heart. At the same time he had generalized abdominal tenderness, the liver was enlarged to the umbilicus, but there was no edema of the extremities. The blood cultures were sterile. The heart was pulsating tumultuously and was grossly irregular. It was not possible to obtain an electrocardiogram to confirm the clinical diagnosis of auricular fibrillation.

Throughout his entire stay at the hospital, he received only four doses of 1.5 cc. of the tincture of digitalis on four separate days. The high fever which occurred with the onset of his last exacerbation of rheumatic fever persisted till one day before death, when the temperature became subnormal.

CHRONIC AURICULAR FIBRILLATION

The most common type of auricular fibrillation in children met with in hospital practice is the chronic or permanent form. We have observed it in five of the children who form the basis of this study. Most frequently the irregularity is ushered in without premonitory symptoms. It may come on insidiously during an active attack of fever or be discovered accidentally in the late stages of decompensation. In two children with chronic auricular fibrillation, the irregularity appeared during an active carditis. In the others, the arrhythmia was noted in the late stages of heart failure. All of the patients in whom it was observed were receiving digitalis at the time of its discovery.

While this arrhythmia in children is compatible with life, it will be seen from the following case reports that it is only with great care and the judicious use of therapeutic measures that existence can be prolonged until finally the heart condition no longer responds to treatment.

CASE 5.—*Chronic rheumatic cardiac valvular disease; mitral stenosis and insufficiency, aortic insufficiency, relative tricuspid insufficiency, premature ventricular beats, bigeminal rhythm, chronic auricular fibrillation.*

L. C., a girl, aged 9, showed the first signs of involvement of the heart at the age of 4. At the age of 7, she had an exacerbation of rheumatic fever and a recurrence of the disease two months before admission to our hospital.

At the first examination on admission to the hospital, she presented, in addition to valvular defects, many premature beats. Nevertheless, because of a large liver, she was placed first on daily doses of 2 cc. of tincture of digitalis, which was soon increased to 4 cc. for a period of two and a half months, when the drug was discontinued because of slowing of the pulse rate which varied from 96 to 50 beats per minute. In the interim, the premature beats had entirely disappeared.

Three months after admission, the patient developed signs of marked heart failure. She became intensely cyanotic and very dyspneic even while lying quietly in bed. At about this time, digitalis was administered to her only when it was thought advisable, since she occasionally showed toxic manifestations from excesses of the drug in the form of a bigeminal rhythm. Examination now revealed diffuse irregular pulsations over the entire precordium. The veins of the neck were distended and showed the ventricular form of venous pulse. The liver was palpable below the umbilicus. It was not tender but pressure over it distended the cervical veins. The heart and pulse rhythms were grossly irregular. The clinical diagnosis of auricular fibrillations was shortly after this confirmed by the electrocardiogram.

All this time her temperature was normal, but subsequently, during the period of auricular fibrillation, she developed signs of active carditis that lasted for four months. Following this period the temperature pursued a subnormal course throughout the period of observation, with the exception of an occasional rise. With the onset of the auricular fibrillation, she developed severe signs of decompensation and ascites, so that repeated paracenteses of the abdomen were necessary for her comfort. In the meantime, she continued to receive daily doses of the tincture of digitalis in doses of from 1 to 2 cc. twice a day. Because the drug in this form had but little effect on her general condition, the tincture was changed to an infusion and administered in daily doses of 12 cc. After six months of the

constant use of the infusion, the tincture was again tried with the hope of relieving the persistent ascites and generalized anasarca. However, the tincture had to be discontinued soon, since the child showed alternate premature ventricular beats when only small doses were administered. From that time on until her discharge from the hospital twenty-one months after the onset of the auricular fibrillation, she received digitalis only when it was thought advisable to lower her ventricular rate.

With the persistent use of digitalis, together with repeated paracenteses, she finally improved sufficiently to permit discharge; but she died suddenly while at home, one month after leaving the hospital.

CASE 6.—*Chronic rheumatic cardiac valvular disease; mitral stenosis and insufficiency, aortic insufficiency, relative tricuspid insufficiency, premature ventricular beats, chronic auricular fibrillation.*

M. G., a girl, aged 10, had her first attack of rheumatic fever at the age of 5, when a diagnosis of heart disease was made. Subsequently for a period of about one month in each year she had attacks of palpitation of the heart, dyspnea, orthopnea and slight edema of the legs. These symptoms improved after rest in bed.

Nine months prior to her admission to the hospital, she was observed at our cardiac clinic, and her heart rhythm was found to be regular. Three weeks before admission, during an exacerbation of rheumatic fever with arthritis, she suddenly became conscious of a rapid thumping in her chest and a "beating in the neck." She vomited and complained of abdominal pains. Because of the abdominal symptoms, a slight rise of temperature and a high leukocyte count, she was admitted to the surgical service of the Fordham Hospital where a diagnosis of auricular fibrillation was made. Two months later she was transferred to Montefiore Hospital.

On admission, she was dyspneic and cyanotic. The heart rate was grossly irregular, the veins in her neck were distended, and there was a marked pulse deficit. The liver extended below the umbilicus and was pulsating. There was no edema of the lower extremities. A clinical diagnosis of auricular fibrillation was confirmed by the electrocardiogram.

During her stay in the hospital, her temperature was practically always subnormal, except for a short period when she showed signs of acute pericarditis. During this period, she became refractory in her response to the tincture of digitalis so that the dose had to be varied from day to day depending on her signs and symptoms. She developed nausea and vomiting with a bigeminal rhythm when the dose was in excess and a rapid ventricular rate when the dose was omitted. Five months after the onset of the auricular fibrillation the girl died with acute pulmonary edema.

CASE 7.[7]—*Chronic rheumatic cardiac valvular disease; mitral stenosis and insufficiency, aortic insufficiency, chronic auricular fibrillation.*

Z. B., aged 12, when admitted to the hospital was known to have had auricular fibrillation for two months. Her past history was one of recurrent attacks of rheumatic fever for seven years. Shortly before admission, the patient was digitalized preparatory to an attempt to restore normal sinus rhythm by means of quinidine.

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7. We are indebted to Dr. David Felberbaum for the privilege of reporting this case.

On the day of admission she received a test dose of 0.2 Gm. of quinidine sulphate, and as no untoward effects were noted, she was given similar doses at three hour intervals the next day. The pulse became slower, but remained irregular. On the third day, she received five doses of 0.2 Gm. each, three hours apart. Her pulse during that day became rapid and very irregular at times, and she complained of some shortness of breath. In the evening her pulse rate was about 100 a minute. The dose of quinidine was not increased until the fourth day after her admission, when she was given 0.45 Gm. every three hours for four doses. On the afternoon of this day, she complained of severe abdominal cramps, but at the same time it was noted that her pulse became regular and remained so until her discharge from the hospital a few days later.

Since she was tolerant to quinidine, the dose of 0.45 Gm. twice a day was continued while the patient was at home. Nevertheless, there was a recurrence of auricular fibrillation about fifteen days after the establishment of normal sinus rhythm, and this continued until her death three years and five months after the appearance of the arrhythmia.

CASE 8.—*Chronic rheumatic cardiac valvular disease; mitral stenosis and insufficiency, aortic insufficiency, relative tricuspid insufficiency, chronic auricular fibrillation.*

L. W., a girl, aged 10, was known to have had heart trouble at the age of 8. At 9, she was tapped for ascites. Half a year later, when she was admitted to our ward, she had severe decompensation. Shortly afterward she developed auricular fibrillation, and between this time and her death, seven months later, it was necessary to perform paracentesis abdominalis on fourteen occasions.

With the exception of one febrile episode of short duration, her temperature was always subnormal during her stay in the hospital. In this girl, the auricular fibrillation appeared with a slow ventricular rate that lasted for several days before it became rapid, but it was finally controlled by effective doses of tincture of digitalis. After this period of slow ventricular action, it was noticed that the rate became increased, despite the fact that she was receiving the same dose of digitalis before, during and after the onset of the arrhythmia.

CASE 9.—*Chronic rheumatic cardiac valvular disease; mitral stenosis and insufficiency, aortic insufficiency, premature ventricular beats, bigeminal rhythm, chronic auricular fibrillation.*

D. C., a boy, aged 13, was known to have had attacks of rheumatic fever since the age of 5. Two years prior to his admission to our hospital, he had severe decompensation with hydrothorax. After a period of rest and the administration of diuretics, he recovered sufficiently to be sent home from the New York Hospital, but had to be readmitted to the same institution several times within the next year because of recurrences and exacerbations of rheumatic fever. On his last admission, he developed auricular fibrillation during an attack of active carditis. When transferred to the Montefiore Hospital he was very sick. His temperature was only slightly elevated at first, but it became higher as the result of bronchopneumonia with signs which persisted for several weeks. During this time he received tincture of digitalis in small doses whenever it was found necessary to control and to slow his ventricular rate.

During the last two months of his illness, the boy became intolerant to effective doses of digitalis. Whereas prior to this time, the usual doses of 2 cc. of the tincture a day were sufficient to keep him comfortable and free from palpitations, the same dose now caused a bigeminal rhythm with many premature ventricular

beats, so that it became necessary to vary the amount of digitalis from day to day depending on the symptoms presented. Eight months after the onset of auricular fibrillation, he died with severe signs of decompensation and ascites.

CASE 10.—Chronic rheumatic cardiac valvular disease; mitral stenosis and insufficiency, aortic insufficiency, chronic auricular fibrillation.

J. D., a girl, aged 15, was known to have had heart disease at the age of 9, and two years later tonsillectomy was advised because of repeated sore throats. Shortly after this, she had to be admitted to the Fifth Avenue Hospital because of an attack of fever. Between that time and the date of admission to our ward she had six separate attacks of fever during one of which it was thought advisable to puncture her maxillary sinuses.

She was admitted to Montefiore Hospital in 1927. A clinical diagnosis of auricular fibrillation was made and was confirmed by the electrocardiogram. During her stay in the hospital, she appeared comfortable and was up and about most of the time. At the present time she is at home doing light housework and is able to maintain adequate compensation without the use of any digitalis, her pulse rate varying between 60 at rest and 85 on severe exertion, such as climbing one flight of stairs.

TABLE 2.—*Data on Authors' Cases*

Case No.	Type of Fibrillation	Patient	Sex *	Age at Onset of Fibrillation, Years	Duration of of Fibrillation Till Death
1	Paroxysmal	A. B.	♂	13½	6 days
2	Terminal	A. J.	♂	8½	3 days
3	Terminal	D. N.	♂	10	3 days
4	Terminal	M. B.	♂	10½	4 days
5	Permanent	L. C.	♀	9	22 months
6	Permanent	M. G.	♀	10	5 months
7	Permanent	Z. B.	♀	12	41 months
8	Permanent	L. W.	♀	10½	7 months
9	Permanent	D. C.	♂	13½	8 months
10	Permanent	J. D.	♀	15	Still alive

* In this table ♂ indicates male and ♀, female.

COMMENT

It would seem from our experiences at the Montefiore Hospital that auricular fibrillation is not uncommon in children with rheumatic heart disease. We believe that the frequency of this irregularity in our series is not due to the fact that they are of a selected or special type, but that its recognition in children depends in a great measure on the care with which the heart rhythm is studied.[8] As a matter of fact, it is our belief that further search may reveal a still greater percentage of auricular arrhythmia (flutter, fibrillation, tachycardia) in children with active rheumatic disease; for it is well known that acute carditis is an almost invariable accompaniment of rheumatic fever in children, and consequently the chances of functional disturbances of the heart rhythm from

8. For example, between 1921 and 1926, only four children with auricular fibrillation were observed on the wards, whereas since the beginning of this study in September, 1926, till December, 1927, we have noted ten children with this arrhythmia.

this disease in itself are great. Undoubtedly, however, in long-standing chronic valvular heart disease in children other factors must be considered among the causes of auricular fibrillation.

It is well known from the researches of Lewis and his co-workers that experimentally the circus movement supposedly underlying the mechanism of auricular fibrillation appears primarily as a result of a strain placed on the auricle by a rapid rate of beating and the consequent increase in partial refractoriness and its concomitant depression of conduction through the auricular musculature. Clinically, it is much more difficult to reconcile the appearance of this abnormal rhythm with certain well defined physiologic and pathologic processes. Nevertheless, in certain of our cases, there seems to be a definite association between (*a*) active rheumatic carditis, (*b*) mitral stenosis and (*c*) the administration of digitalis on the one hand and the development of auricular fibrillation on the other. Before discussing these conditions, however, it is worth while to consider any extrinsic factors that might be held responsible for initiating auricular fibrillation.

Extrinsic Factors and the Development of Auricular Fibrillation.—We have been unable to find from our data any clinical or graphic criteria which would enable us to predict which of the children with chronic rheumatic valvular heart disease will become the subjects of auricular fibrillation. Predisposing factors such as trauma, heart strain, excessive effort and emotional disturbances, frequently associated with the onset of auricular fibrillation in adults, did not play any rôle in the children observed, for all of our patients were bedridden at the time the irregularity was noted in them. In none did we observe any chronic gastric or intestinal disorder that might be associated with the direct onset of the arrhythmia, nor have we been able to deduce any relationship between preexisting functional disturbances of rhythm such as premature beats and block and subsequent auricular fibrillation in one and the same patient.

In his earlier work on gross arrhythmia of the auricles, Lewis [9] noted in patients with paroxysmal auricular fibrillation the presence of isolated beats interrupting the periods of normal rhythm prior to the onset of the arrhythmia. In support of this clinical observation, he has shown experimentally that the circus movement in the auricle is provoked when an effective stimulus enters its muscle in the partial refractory state.[10] A premature beat of the auricle may be considered

9. Lewis, T.: Auricular Fibrillation and Its Relationship to Clinical Irregularity of the Heart, Heart **1**:306, 1909-1910.

10. Lewis, T.; Drury, A. N., and Bulger, H. A.: The Refractory Period and Rate of Propagation in the Auricle, Heart **8**:83, 1921.

an effective stimulus. While such factors hold true for some patients with paroxysmal auricular fibrillation, they have played no rôle in the children we have studied.

Acute Rheumatic Carditis and the Development of Auricular Fibrillation.—Rheumatic carditis per se has never been accepted as a cause of auricular fibrillation in spite of the fact that a number of cases of this irregularity occuring in adults at the height of an attack of rheumatic fever have been reported.[11] In this paper, we add six additional cases in children. The possibility of rheumatic carditis causing auricular fibrillation in children has been questioned on grounds that some of the cases reported might have been complicated by septic endocarditis at the time the irregularity was noted.[12] This is specious reasoning, for infectious endocarditis rarely occurs in a heart the auricles of which are permanently fibrillating. The fact that we have observed auricular fibrillation in six of our cases should dispel the idea of its rarity or absence in children during the active stages of rheumatic fever. It is impossible to prove that the infection in itself is responsible for the development of the fibrillation of the auricles but the association is suggestive.

It may be questioned that in one of our children who had bronchopneumonia as a complication, the signs in the lung dominated the picture, and that the auricular arrhythmia discovered during that time was a manifestation of the severe pulmonary complication rather than the definite evidence of an active rheumatic cardiac involvement. Recent careful studies of cases of children with autopsy observations made by Boas and Schwartz [5] have shown that in such patients with chronic rheumatic valvular heart disease, the gradations from pneumonia to acute rheumatic carditis are so imperceptible clinically that they were inclined to consider the entire picture as the result of rheumatic fever. In other words, it was not the pneumonia per se, but the generalized rheumatic infection of which pneumonia was one of the signs that we feel was responsible for the fibrillation in this particular child.

Mitral Stenosis and the Development of Auricular Fibrillation.—The older clinicians were keenly appreciative of the close association between

11. Krumbhaar, E. B.: Transient Auricular Fibrillation: An Electrocardiographic Study, Arch. Int. Med. **18**:263 (Aug.) 1916. Levine, S. A.: Auricular Fibrillation: Some Clinical Considerations, Am. J. M. Sc. **154**:43, 1917. Laubry, C., and Doumer, E.: Arrythmie complete au course d'un rhumatisme articulaire aigu-regularisation par la quinidine, Bull. et mém. Soc. méd. d. hôp. de Paris **46**: 1287, 1922. Cohn, A. E., and Swift, H. F.: Electrocardiographic Evidence of Myocardial Involvement in Rheumatic Fever, J. Exper. Med. **39**:1, 1924. Rothschild, M. A.; Sacks, B., and Libman, E: Disturbances of Cardiac Mechanism in Subacute Bacterial Endocarditis and Rheumatic Fever, Am. Heart J. **2**:371, 1927.

12. Parkinson, J.; Gosse, A. H., and Gunson, E. B.: The Heart and Its Rhythm in Acute Rheumatism, Quart. J. Med. **13**:363, 1919-1920.

mitral stenosis and an "arrhythmic pulse," and long before the mechanism of auricular fibrillation was ever suspected, the "mitral" pulse had an ominous prognostic significance. This was thought to be true particularly in patients who gave a history of swollen and painful joints and who had marked dropsy, or in children who were the subjects of periodic attacks of chorea and who had evidence of a heart lesion. We now know too well that over 35 per cent of adults with mitral stenosis become the victims of auricular fibrillation. The figures may be somewhat smaller in children, but the condition is infinitely graver. All of the children in this series had mitral stenosis.

Several interpretations have been suggested as possibly explaining the high incidence of auricular fibrillation with this condition. According to Lewis [9] the purely mechanical doctrine of increased intra-auricular pressure is untenable because auricular fibrillation may occur in many cases where increased intra-auricular pressure may not be assumed. Nor can the sudden distention of the auricles in themselves be responsible for the onset of the arrhythmia.[13] Again, auricular fibrillation has from the beginning of its study been attributed to definite pathologic changes in the musculature of the auricle or the specialized tissue of the sino-auricular node. Yet, there are numerous cases in which it has been impossible to demonstrate any anatomic changes in these regions that could be associated with auricular fibrillation. Nevertheless, Wilson [14] still believes that persistent auricular fibrillation is invariably associated with chronic changes in the heart muscle which are not readily demonstrable by our present known anatomic methods. These changes may be physicochemical, and it is likely that some such changes might also explain the relationship of paroxysmal fibrillation in patients with exophthalmic goiter. (In this connection we should mention the fact that so far as we know and from personal communication with Dr. David Marine, fibrillation of the auricles has never been observed in children with exophthalmic goiter.)

Digitalis and the Development of Auricular Fibrillation.—The onset of auricular fibrillation in adults with myocardial failure has at times been associated with the administration of excessive doses of digitalis. This relationship though suspected, has not been proved for permanent auricular fibrillation.[15] It is possible, however, as has been recently

13. Wenckebach, K. F., and Winterberg, H.: Die unregelmässige Herztätigkeit, Leipzig, 1927, pp. 441-467.

14. Wilson, F. N.: Auricular Fibrillation, J. Michigan M. Soc. **22**:478, 1923.

15. Mackenzie, J.: Digitalis, Heart **2**:273, 1910-1911. Cushny, A. R.: Therapeutics of Digitalis and Its Allies, Am. J. M. Sc. **141**:469, 1911. Danielopolu, D.: Arrythmie complete chez l'homme provoquee par la digitale: rôle du système moderateur, Compt. rend. Soc. de biol. **79**:97, 1916. Reid, W. D.: Some Toxic Effects of Digitalis, J. A. M. A. **81**:435 (Aug. 11) 1923.

shown by Resnik [16] to induce a transient type of auricular fibrillation by the administration of effective doses of a potent preparation of the drug. In seven patients with severe myocardial failure in whom he was able to produce auricular fibrillation by this method, restoration to normal sinus rhythm took place in every instance after the drug was discontinued. On the basis of these experiences, the following criteria were offered for judging whether a causal relationship exists between the onset of auricular fibrillation and excessive digitalis therapy.

(1) A history must be obtained that previous attacks of auricular fibrillation were absent.
(2) Normal rhythm must be present before digitalis is administered.
(3) Auricular fibrillation must appear after an effective dose of digitalis as judged by clinical and electrocardiographic evidence.
(4) The normal rhythm must be clearly established by electrocardiographic records.
(5) Other factors which tend to bring on transient auricular fibrillation must be eliminated.

In confirming these criteria of Resnik on paroxysmal auricular fibrillation following overdigitalization, we have observed that the abnormal rhythm may persist several days after the drug has been discontinued and restoration to normal sinus rhythm may not take place until most of the digitalis bodies have been excreted from the system. Furthermore, it has been our experience that the development of auricular fibrillation during the administration of this drug has always been accompanied by a slow ventricular rate when alternate premature beats were not present.

In the light of these observations, the only reported protocols of children in whom this phenomenon was studied prior to our own observation bear repetition since they have apparently escaped notice.

In 1913, Nadel [17] followed the case of a boy, aged 11, who was suffering from chronic rheumatic valvular heart disease. In normal times the pulse was regular and the electrocardiograms revealed in addition to the characteristic preponderance of the right ventricle associated with mitral stenosis, a large notched P wave and a prolongation of the P-R interval to 0.2 seconds.

During the administration of digitalis for severe decompensation in this child, Nadel studied by means of graphic methods a successive series of irregularities that appeared from what seemed to him to have been the excessive use of the drug. The arrhythmia was always paroxysmal in type and was closely related to the time when digitalis

16. Resnik, W. G.: Transient Auricular Fibrillation Following Digitalis Therapy with Observations upon the Reaction of Atropine, J. Clin. Investigation **1**:181, 1924-1925.

17. Nadel (footnote 4, first reference).

was known to have accumulated in the circulatory system. One day there was definite slowing and the heart rate dropped to almost one-half the normal from its original. On another day, there appeared premature ventricular beats, and frequently these were coupled so as to give rise to a bigeminal rhythm. Without any accompanying symptoms, there appeared on another day definite evidences of transient auricular fibrillation. The ventricular rate during this time was slow averaging only 66 beats per minute without the numerous premature beats that brought it up to 74. Unfortunately this brief report of Nadel's lacks in further details that would enlighten us on the fate of this child.

In 1920, Neuhoff [18] observed a boy, aged 8, with mitral insufficiency and heart failure but an otherwise regular heart rhythm. Every time the boy was under the maximum effects of digitalis, auricular fibrillation developed. Polygraphic tracings left no doubt as to the type of arrhythmia. Neuhoff tried the digitalis experiment several times. When the drug was discontinued fibrillation stopped and the pulse became regular at the end of a day or so; when it was again administered, the auricles again fibrillated.

In our own case (case 1), the period of transient auricular fibrillation appeared and passed at a time when digitalis was being administered in excessive doses. The bigeminal rhythm recorded simultaneously with the auricular arrhythmia may be taken as evidence, in addition to the foregoing criteria, that the development of the irregularity was closely associated with excessive digitalis therapy. The dose does not matter, for it is well known that children react differently to the drug under varied conditions. A small dose which is well tolerated at one time may be highly toxic at another. Again the fact that in this boy restoration of normal sinus rhythm occurred at a time when digitalis was still being administered corroborates our conception that the abnormal rhythm may appear during the cumulative actions of the drug and pass away when not enough of the drug is present in the system.

While these unusual instances show the development of paroxysmal auricular fibrillation to be closely associated to digitalis therapy, further studies are required to prove that other types of fibrillation discussed in this paper are similarly produced in children with advanced myocardial failure. No attempt is made here to describe the mechanism whereby this particular drug is able to cause the onset of auricular fibrillation.

DIFFERENTIAL DIAGNOSIS

A marked sinus arrhythmia with multiple premature auricular and ventricular beats, many of which are not felt at the pulse because of their

18. Neuhoff (footnote 4, fourth reference).

inability to open the aortic valves during the incomplete filling of the ventricles, may readily be confused with auricular fibrillation. Auricular premature beats, as is well known, may be unaccompanied by compensatory pauses so that with a vagus arrhythmia present, the irregularity as observed both at the apex of the heart and at the wrist resembles auricular fibrillation with a pulse deficit. (This has to be borne in mind because of the frequency of sinus arrhythmia in children.) We have observed two such cases for over two years both in children under 6 years of age. These children have been repeatedly sent to our laboratory with a clinical diagnosis of auricular fibrillation. The electrocardiogram, however, revealed marked sinus irregularity with multiple premature beats, and the freedom of these children from any valvular disease, their remarkable tolerance for exercise, and the disappearance of the premature beats over a prolonged period of time, have confirmed the innocence of this type of irregularity.

In unusual instances, the influence of the vagus on the sinus node may be strong enough to cause a complete cessation of the heart beat with consequent escape of the ventricle. In the electrocardiogram, the iso-electric line produced as a result of nonactivity of the heart preceding this escaped ventricular complex may simulate auricular fibrillation. This we have observed in one of our cases. In these instances, the application of direct leads over the second and fourth intercostal spaces to the right of the sternum in the region of the auricles will obviate the error in diagnosis. If there is any auricular activity present, then by this means there is magnification of the small auricular waves in the electrocardiogram.

Again, the onset of a rheumatic episode in children may be ushered in by the dropped beat phenomenon. This irregularity is produced by a progressive increase in the conduction interval between the auricles and the ventricles, with final failure of the ventricular response to a preceding auricular beat giving rise to a sudden interruption of the normal rhythm, the so-called Luciani or Wenckebach periods. In the presence of a sinus arrhythmia and a rapid ventricular rate, this type of irregularity has been mistaken for fibrillation of the auricles. Fortunately, in children this is a transient incident in the development of rheumatic carditis and passes within a day after its onset.

More rarely, as in case 1, a paroxysm of fibrillation may be masked completely by the presence of alternating premature beats coming at such intervals that the underlying auricular arrhythmia gives but little, if any, clinical evidence. In such cases as well as in those showing complete auriculoventricular dissociation, auricular fibrillation may be recognized only through the use of graphic methods.

TREATMENT

The paroyxsmal and terminal type of auricular fibrillation do not admit of any rational treatment.

In the children with permanent auricular fibrillation, the most important problem is to maintain an adequate circulation so as to prevent breathlessness, severe decompensation and the accumulation of fluid in the serous cavities. In this respect while rest and adequate digitalization may control the ventricular rate, it is almost invariably necessary, as our protocols reveal, to perform both thoracentesis and paracentesis abdominalis from time to time for relief of symptoms. It has been our policy at the times when these measures have been instituted to place the child on restricted fluids for a period of about three days, and help elimination by the intramuscular administration of sodium mercurisalicylallylamido acetate in doses of 1 cc. repeated at twenty-four hour intervals twice. As many as 3,500 cc. of urine have been obtained in one day by such methods with no untoward systemic effects and with great relief to the patient. It is best to vary the digitalis from day to day so as to prevent toxic effects from excessive accumulation.

Quinidine, in adequate amounts, may produce restoration of normal sinus rhythm as has been described in one case (7). However, as in the child quoted by Ogden,[19] the restoration to normal rhythm is only temporary.

PROGNOSIS

In our series of ten children, four died within one week after the onset of the auricular fibrillation, three died within one year, one lived twenty-two months, one survived almost four years and another, who had passed the stage of childhood, is still living although badly crippled by heart disease.

From these figures we gain the impression that auricular fibrillation in childhood is of grave prognostic significance. As is well known, the hearts of children prone to rheumatic infections bear the brunt of the rheumatic virus with each recurrence and exacerbation of the disease. If death does not occur during one of the severe attacks of fever, then in those children with more numerous attacks there is no chance for the myocardium to recuperate before another infection takes place. Consequently, when an abnormal rhythm sets in to add to the burden of an already damaged myocardium, progressive decompensation results, and it is only a question of time before death ensues, no matter what therapeutic measures are instituted for relief. Once this childhood stage is passed, however, the rheumatic infection assumes a different aspect and the prognosis is infinitely better.

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19. Ogden (footnote 4, sixth reference).

In only one child did we observe any embolic complications that resulted in hemiplegia. These are indeed unusual in children. In one other child we noted pulmonary edema as a fatal accompaniment probably causing death by asphyxia. The latter complication is of unusually grave prognostic significance.

CONCLUSIONS

Auricular fibrillation is not rare in children with chronic rheumatic valvular heart disease. Of sixty children observed during a period of five years, ten developed auricular fibrillation. Five of the children were boys and five girls. The auricular fibrillation may be (1) paroxysmal, (2) terminal or (3) chronic in type. Mitral stenosis, acute rheumatic fever and the excessive administration of effective doses of the tincture of digitalis are all factors in the development of auricular fibrillation in children. The prognosis in children with this form of irregularity is grave. In our series of ten children, four died within one week after the onset of the arrhythmia, three died within one year, one lived twenty-two months, and one child who is still living is over 15 years of age now. Pulmonary edema in the course of auricular fibrillation is a grave complication. In one child, hemiplegia was observed as a complication during the presence of auricular fibrillation. The treatment for this arrhythmia in children consists in rest, the control of the ventricular rate with sufficient amounts of digitalis and the elimination of fluids accumulated in the body tissues and serous cavities by the usual procedures of diuretics, diet and paracentesis.

CYTOLYSIS IN THE CEREBROSPINAL FLUID IN ACUTE POLIOMYELITIS *

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An attempt has been made to study the effect of the lapse of time on the cell count of the cerebrospinal fluid in the preparalytic stage of acute poliomyelitic infection. The study has yielded results that suggest the presence of some cytolytic factor particularly active toward the multilobed cells which has not been described previously. The literature has been reviewed, and an effort has been made to explain why conflicting views have been held regarding the advisability of immediate cell counts in all cases in which lumbar puncture is performed for diagnostic purposes.

Wynn,[1] after examining eighty specimens of spinal fluid up to fifteen hours after lumbar puncture, concluded that the cells in clear fluids collected in clean test tubes and tightly stoppered might, in the absence of macroscopic pellicle, sediment or web, and if thoroughly mixed, be safely counted at any time up to fifteen hours. Amoss [2] and others have had essentially the same experience in determining the effect of the elapse of time on the spinal fluid cell count in cases of syphilis of the central nervous system. It is noteworthy that in Wynn's work the counts were made almost without exception in conditions in which there was a mononuclear pleocytosis. The acute poliomyelitic fluids in his series did not show the high cell count often found in the early stages of that infection. Mention was not made in his report of the kind of cells counted.

Bigelow [3] cited the early dissolution of erythrocytes and polymorphonuclear leukocytes with preservation of the lymphocytes in cases of hemorrhage into the cerebrospinal fluid. Except for this observation, all other studies in his series were made on the mononuclear type of pleocytosis.

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* Received for publication, Jan. 25, 1928.

* From the Department of Child Hygiene, Marshall College.

1. Wynn, J.: Effect of Time Between Obtaining a Spinal Fluid and Making a Cell Count on Result of Count, J. Lab. & Clin. Med. **7**:273 (Feb.) 1922.

2. Amoss, H. L.: Personal communication to the author (Oct. 28, 1927) citing work done in the New York State Board of Health Laboratories on cell counts in syphilitic spinal fluids made at the bedside and after they were mailed to the central laboratory.

3. Bigelow: Cytology of the Cerebrospinal Fluid, Cleveland M. J. **14**:196, 1915.

He further stated:

> It is not safe to delay the examination of the spinal fluid six hours after it has been obtained, as experiment has shown that after six hours there is an average decrease of 13 per cent of the number of cells and after twelve hours a decrease of 40 per cent. This is probably due to the destructive action of the fluid, which, as explained before, is constantly reducing the number of cells. Whether this process is swifter "in vitro" is difficult to determine, as one has no means of measuring the accession of cells from the meninges while the fluid is in contact with them.

Morabito [4] has described "autolysis" in spinal fluids. He found that when the fluid was placed in the incubator "spontaneous cytolysis" occurred in from six to forty-eight hours, and that when it was placed in the icebox, it occurred in from nine to 180 hours. He further pointed out that two drops of glacial acetic acid for each cubic centimeter of the spinal fluid, added at the time of puncture, prevented cytolysis.

Rous,[5] in speaking of the disappearance of the cells in the spinal fluid, said:

> The autolytic digestion of leukocytes is now well understood and there seems nothing against self digestion of those of the cerebrospinal fluid (which itself contains no enzymes), provided they are not too speedily hurried into the lymph stream.

Levinson [6] and others [7] pointed out that cells from the cerebrospinal fluid do not stain as well with the ordinary blood stains as do the cells in the blood.

In spinal fluids that are allowed to stand, Rous [5] demonstrated a progressive change in the staining reactions of the cells. He observed this change in normal fluids and in those of tuberculous meningitis. After standing for four hours, either in the room or in the incubator, the lymphocytes regularly showed a change in the staining reaction to Hasting's stain, the distinction between nucleus and protoplasm being lost. Such results suggest a chemical activity, at least within the cells.

Wynn [1] was able to repeat a mononuclear cell count of 2,500 in the fluid from a case of syphilitic meningitis up to fifteen hours after puncture. He was able to repeat a count of 2,000 cells, mainly polymorphonuclear, in a case of pneumococcus meningitis when only a few crystals of sodium citrate were in the tube at the time the fluid was withdrawn.

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4. Morabito, F.: Autocytolysis in Cerebrospinal Fluid, Pediatria (Naples) **34**:1162 (Nov. 1) 1926; abstr., J. A. M. A. **88**:443 (Feb. 5) 1927.

5. Rous, F. P.: Clinical Studies on Cerebrospinal Fluid, Am. J. M. Sc. **133**: 567, 1907.

6. Levinson, A.: Cellular Elements of the Cerebrospinal Fluid, J. Lab. & Clin. Med. **7**:626 (July) 1922.

7. Draper, G.: Acute Poliomyelitis, Philadelphia, P. Blakiston's Son & Company, 1917, p. 71.

In the purulent meningitides accompanied by a polymorphonuclear pleocytosis, there is usually so much fibrin present that an accurate count can be obtained only immediately after puncture. Coagulation, web or pellicle formation often occurs so quickly that the fluid may be worthless from the standpoint of a total count by the time the laboratory is reached. At times, the same condition may occur in tuberculous meningitic fluids. It is rare for a pellicle to form in the fluid in early acute poliomyelitis, especially in the earliest stages of meningeal invasion when the pleocytosis is apt to be greatest and the globulin content relatively low. Wynn reported this as having happened in all of his poliomyelitic fluids with a cell count of over 100, and he ascribed the fall in cell count in his series of fluids to this factor. I have not seen pellicle formation in a fluid from a case of acute poliomyelitis, and according to the literature it apparently does not occur frequently and seldom as frequently as in 60 per cent of the cases, as in Wynn's series.

Amoss [2] and Dochez [8] at the Rockefeller Institute observed a definite decrease in the cell count in cases of acute poliomyelitis when the count was made immediately after puncture and the fluids then allowed to stand and the counts repeated at the end of half an hour and again at the end of one hour. They felt that in all probability it was due to mechanical causes, such as agglutination, sedimentation, adhering to the sides of the glassware, etc. They observed fragmentation in many cells after agitation of the fluid. They found that thorough agitation failed to bring the counts made at the half hour and hour intervals up to the counts made immediately after puncture. These observations were not published but undoubtedly had great influence on the members of this group of workers, as they have consistently advocated immediate "bedside" counts of the spinal fluid in all cases of suspected poliomyelitis.

Draper [7] described a pleocytosis occurring in the earliest period of meningeal invasion in acute poliomyelitis, in which the cells are mainly multilobed in type. By the end of from twenty-four to thirty-six hours, the small mononuclear cells may constitute 90 per cent of the total pleocytosis. Wynn probably did not have fluids from this type of case in his series, as the total cell counts seem too low. He failed to mention the kind of cells counted, and differential counts were not given. All of the studies in my series were made on fluids taken from cases of this class of pleocytosis, early in the preparalytic stage. They are therefore not strictly comparable with those of Wynn's series.

CHARACTER OF FLUIDS STUDIED

The spinal fluids studied were obtained from three poliomyelitic patients, aged 2½, 2 and 4 years, respectively. The first fluid in each case was obtained near the beginning of the "second hump" (Draper).

8. Dochez, A. R.: Personal communication to the author (Nov. 3, 1927).

This period coincides closely with the beginning of the central nervous system phase of the infection. At the time of the first lumbar puncture, all three cases presented clinically the earliest signs of meningeal invasion. The signs appeared so suddenly and were so severe that a malignant purulent meningitis was strongly suspected. Paralysis first appeared after thirty, fifty-four and sixty-six hours, respectively. Each patient presented an early pleocytosis of high degree, characterized by a high multilobed cell count which fell quickly, as described by Draper [7] and others.[9] By the time the paralysis appeared, the cells were almost entirely of the mononuclear type with a pleocytosis of only moderate grade. There are no reports in the literature on the effect of the elapse of time on the cell count in fluids from such cases. All reported studies seemingly have dealt with fluids of a lower cell count in which the pleocytosis has invariably been mononuclear.

TECHNIC

Manner of Obtaining Fluid.—The glass test tubes and ordinary corks to fit were cleansed without soap, in very hot tap water, rinsed several times with distilled water and then sterilized in a steam bath. The tubes were then tightly stoppered with the corks and kept sterile. Three tubes were used at each puncture. In the first tube was collected the first 4 or 5 cc. of the spinal fluid, and this was used for chemical analysis. In the second tube was collected about 10 to 15 cc. of the fluid. From this was immediately taken the fluid for the first cell count. It was made at the bedside while the assistant attended to the puncture wound. Then before the fluid had time to change or the cells to settle out, the fluid from the second tube was divided about equally between the second tube (T2) and the third tube (T3), and both were tightly stoppered.

Management of the Fluid.—The second tube (T2) of each series was allowed to stand at room temperature, about 15 to 30 C., and the counts made and recorded as shown in tables 1, 2 and 3.

The third tube (T3) of each series was placed in the incubator at a temperature of 38 C., and subsequent counts made and recorded as shown in tables 1, 2 and 3.

Selection of a Method of Agitation.—An attempt was made to use a method of agitating the fluids that would introduce a minimal source of error.

Some fluid from an early puncture in one of the patients (case 3, fluid 3) was studied as follows: At puncture a count was made on about 8 cc. of the fluid. Then the fluid was about equally divided into each of two test tubes prepared as I have described for the collection of spinal fluid. Each was immediately stoppered with a clean, smooth cork. Tube A was vigorously shaken for two or three minutes and a counting preparation made. Tube B was gently inverted several times to the minute, meanwhile being rotated between the fingers in such a manner that there was a gentle prolonged agitation of the fluid which was kept

9. Army Medical Manual, no. 6, ed. 2, Philadelphia, Lea & Febiger, 1919, p. 73. Holt and Howland: The Diseases of Infancy and Childhood, ed. 9, revised, New York, D. Appleton & Company, 1926, p. 674.

up for at least five minutes. Then a counting preparation was made. The total counts were almost identical; a little fragmentation was seen in tube A but none in tube B.

At the end of six hours, both tubes were gently inverted two or three times and a counting chamber preparation made from each to observe clumping. Clumping was noticed in both tubes, but it was not extensive. Then each tube was agitated as it had been six hours previously, and the cell count was repeated. Again the total count was practically the same. Almost no clumping was seen in either preparation. Considerable fragmentation occurred in tube A, but little in tube B. While the total counts were essentially the same, fragmentation in

TABLE 1.—*Record of Counts Made Showing the Influence of Elapsed Time and Temperature on the Cell Count of the Spinal Fluid in Case 3*

Fluid	Cells per C.Mm.	Multilobed Cells		Mononuclear Cells		Time Interval in Hours	Temperature
		Per Cent	Per C.Mm.	Per Cent	Per C.Mm.		
1	1,000	62	620	38	380	0	
2	460	46	212	54	248	0	
3 A	262	34	89	66	173	0	
B	228	..	...	..	...	½	Room
	208	..	...	..	...	½	Incubator
C	202	20	40	80	162	2	Room
	166	16	26	84	140	2	Incubator
D	150	..	...	..	...	6	Room
	108	..	...	..	...	6	Incubator
E	120	7	8	93	112	12	Room
	82	0	0	100	82	12	Incubator
4 A	85	10	10	90	76	0	
B	76	1	1	99	75	1	Room
	68	0	0	100	68	1	Incubator
C	72	0	0	100	72	2	Room
	60	0	0	100	60	2	Incubator
D	62	0	0	100	62	6	Room
	54	0	0	100	54	6	Incubator
E	58	0	0	100	58	12	Room
	50	0	0	100	50	12	Incubator
5 A	30	0	0	100	30	0	
B	26	0	0	100	26	2	Room
	22	0	0	100	22	2	Incubator
C	22	0	0	100	22	6	Room
	18	0	0	100	18	6	Incubator
D	16	0	0	100	16	12	Room
	12	0	0	100	12	12	Incubator

In the tables, room temperature indicates 15 to 30 C.; incubator temperature, 38 C.

tube A rendered the differential count in this fluid unsatisfactory by increasing greatly the number of cells that could not be classified. This procedure was repeated and the observations confirmed on a fluid taken from another patient (case 4, fluid 1). This fluid showed a high cell count consisting mainly of multilobed cells.

Accordingly, the method chosen for the present study was that employed in the case of tube B, which consisted of prolonged gentle agitation.

Technic of Making the Cell Counts.—The fluid for the cell count was taken from the center of the specimen. In the higher cell counts, it was necessary to make counts with the aid of diluting fluids. In some cases it was found best to dilute the fluid with equal parts of Turck's solution (1 per cent aqueous gentian violet 1 cc., glacial acetic acid 1 cc., distilled water 100 cc.), to which had been added

a trace of methylene blue. In other cases it was necessary to make the count using a dilution of one part of Turck's solution to three parts of fluid. All other counts were made in the manner described.

Two white cell pipets were used in making each count. They were cleansed in the usual manner with water, alcohol and ether. No further preparation was

TABLE 2.—*Record of Counts Made Showing the Influence of Elapsed Time and Temperature on the Cell Count of the Spinal Fluid in Case 4*

Fluid	Cells per C.Mm.	Multilobed Cells		Mononuclear Cells		Time Interval in Hours	Temperature
		Per Cent	Per C.Mm.	Per Cent	Per C.Mm.		
1 A	1,200	63	756	37	444	0	
B	980	54	529	46	451	1	Room
	900	51	459	49	441	1	Incubator
C	840	46	386	54	454	2	Room
	750	45	338	55	412	2	Incubator
D	688	41	282	59	406	6	Room
	554	29	161	71	393	6	Incubator
E	560	39	218	61	342	12	Room
	430	27	116	73	314	12	Incubator
2 A	500	50	250	50	250	0	
B	440	44	194	56	246	1	Room
	400	41	164	59	236	1	Incubator
C	370	34	126	66	244	2	Room
	325	33	107	67	218	2	Incubator
D	300	24	72	76	228	6	Room
	238	13	31	87	207	6	Incubator
E	275	34	93	66	182	12	Room
	200	25	50	75	150	12	Incubator
3 A	156	18	28	82	128	0	
B	136	14	19	86	117	1	Room
	128	15	12	88	113	1	Incubator
C	124	11	14	89	110	2	Room
	100	10	10	90	90	2	Incubator
D	112	10	11	90	101	6	Room
	88	15	13	85	75	6	Incubator
E	110	9	10	91	100	12	Room
	80	10	8	90	72	12	Incubator
4 A	62	0	0	62	100	0	
B	58	0	0	58	100	1	Room
	50	0	0	50	100	1	Incubator
C	50	0	0	50	100	2	Room
	42	0	0	42	100	2	Incubator
D	46	0	0	46	100	6	Room
	37	0	0	37	100	6	Incubator
E	46	0	0	46	100	12	Room
	37	0	0	37	100	12	Incubator
5 A	45	0	0	45	100	0	
B	42	0	0	42	100	2	Room
	34	0	0	34	100	2	Incubator
C	42	0	0	42	100	12	Room
	34	0	0	34	100	12	Incubator

made on the first pipet, and the second was prepared as follows: Glacial acetic acid, deeply stained with methylene blue, was drawn up to the 1 mark and expelled. The excess was removed by holding the capillary tip against a blotter and forcing air through the pipet. That part of the pipet which had been in contact with the acid was then wiped as free from acid as possible with moist cotton.

In quick succession the fluids were then drawn into the pipets, the one which had not been in the acid being used first. Counting preparations were then made

in Thoma-Levy hemacytometers, two preparations being made from each pipet. The nine larger squares of each preparation were counted and this number multiplied by 10/9. The total counts were made with the low power lens. The differential counts were made with the high dry lens, the preparation that was acidulated and stained being used. The total counts obtained in the undiluted fluids corresponded closely with the counts in the acidulated fluids. The small amount of glacial acetic adhering to the capillary pipet does not materially affect the total count.

Red cells were not encountered at any time in the fluid in this series. This is considered a matter of good fortune, as the presence of red cells cannot be avoided at times. It will be seen from the methods described that much effort has

TABLE 3.—*Record of Counts Made Showing the Influence of Elapsed Time and Temperature on the Cell Count of the Spinal Fluid in Case 5*

Fluid	Cells per C.Mm.	Multilobed Cells		Mononuclear Cells		Time Interval in Hours	Temperature
		Per Cent	Per C.Mm.	Per Cent	Per C.Mm.		
1 A	900	59	531	41	369	0	
B	840	55	462	45	378	1	Room
	770	52	400	48	370	1	Incubator
C	745	50	373	50	372	2	Room
	660	47	310	53	350	2	Incubator
D	590	39	230	61	360	6	Room
	460	32	147	68	313	6	Incubator
E	440	23	101	77	339	12	Room
	320	15	48	85	272	12	Incubator
2 A	338	49	166	51	172	0	
B	306	49	150	51	156	1	Room
	264	40	106	60	158	1	Incubator
C	270	40	108	60	162	2	Room
	238	35	83	65	155	2	Incubator
D	160	0	0	100	160	6	Room
	104	0	0	100	104	6	Incubator
E	106	0	0	100	106	12	Room
	82	0	0	100	82	12	Incubator
3 A	90	0	0	100	90	0	
B	85	0	0	100	85	2	Room
	78	0	0	100	78	2	Incubator
C	63	0	0	100	63	12	Room
	58	0	0	100	58	12	Incubator

been put forth to avoid the introduction of disturbing factors, whether physical or chemical.

The tables give the cell counts as made and recorded. The charts give the curves expressing the fall in cell count that occurs when the fluid is allowed to stand, the relation of the first or immediate cell counts in each case and its relation to the onset of paralysis in a series of eight cases and also the curves expressing the average of Wynn's [1] cell counts.

It is a matter of frequent observation that the spinal fluid cell counts in acute poliomyelitis often fall before paralysis appears. This observation is recorded in chart 4. The sudden pleocytosis, mainly multilobed, quickly falls and is replaced by a lower cell count made up almost entirely of mononuclear cells. This entire fluid and cellular reaction, which is suggestive of a single sudden massive showering of virus into

the cerebrospinal fluid, may be considered pathognomonic of acute poliomyelitic infection. It has not been observed in any other condition. It is also interesting to note that the fall in cell count occurs just about as rapidly "in vivo" as it does "in vitro." This is shown in charts 1, 2 and 3.

In the light of Wynn's series, it may be easy for some to feel that it is not necessary to make the cell counts at the bedside. The counts presented in the present series and the observations of Amoss [2] and his co-workers are confirmatory of the generally held belief that when lumbar puncture is performed for diagnostic purposes, cell counts should

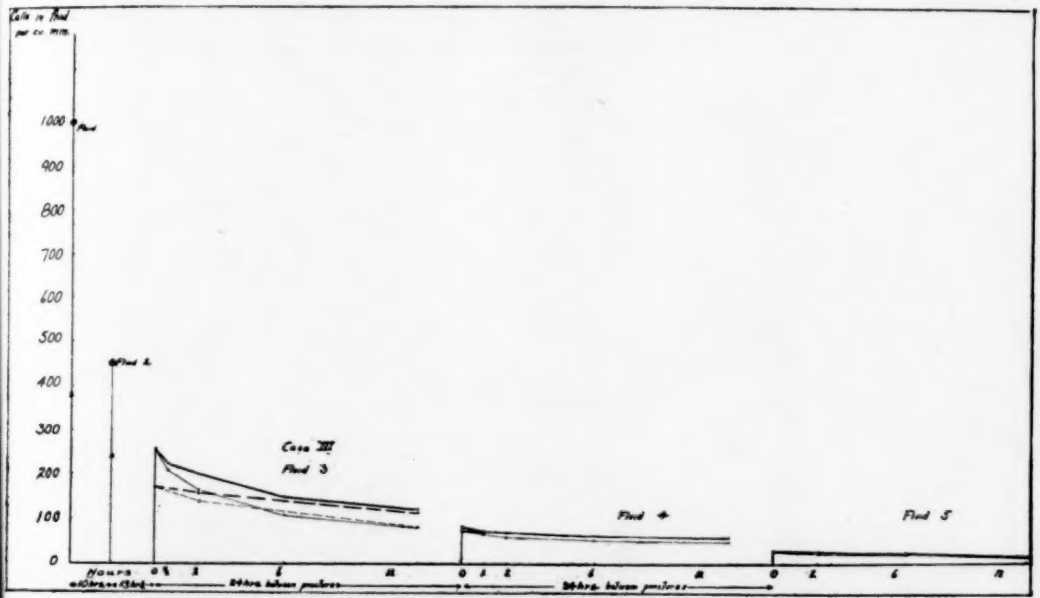

Chart 1.—Cytolytic action of spinal fluid in acute poliomyelitis. The dark continuous line represents the total cell count with the fluid kept at room temperature, 15 to 30 C.; the dark dash line, the mononuclear count with the fluid at the same temperature; the lighter continuous line represents the total cell count with the fluid kept in an incubator at 38 C.; the lighter dash line, the mononuclear count with the fluid kept in an incubator at the same temperature. Special studies were not made on fluids 1 and 2.

be made immediately. Furthermore, there is no discrepancy between the lower counts in my series and the higher counts in Wynn's series, as can be seen by comparing the curves of my series (charts 1, 2 and 3) with those representing his series (chart 5). There is a close correspondence in these counts. They were probably taken from spinal fluids in relatively the same period or phase of the infection.

COMMENT

The origin of the cellular elements of the cerebrospinal fluid in normal and in pathologic conditions has not been fully determined. The multilobed cells, which increase early in acute poliomyelitis, may be identical with the polymorphonuclear leukocytes of the blood stream. Levinson [10] described them as "polymorphonuclear leukocytes." Draper [7] said that they are the wandering clasmatocytes of Marchand and are not necessarily of hematogenous origin. This seems to be the more common belief.

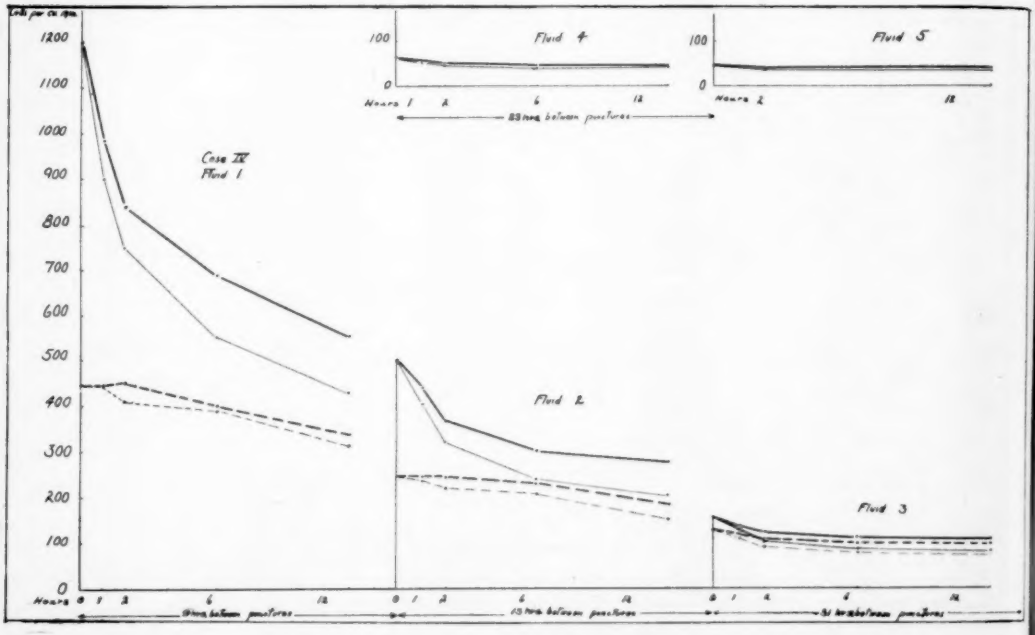

Chart 2.—Cytolytic action of spinal fluid in acute poliomyelitis. The dark continuous line represents the total cell count with the fluid kept at room temperature, 15 to 30 C.; the dark dash line, the mononuclear count with the fluid kept at the same temperature; the lighter continuous line represents the total cell count with the fluid kept in an incubator at 38 C.; the lighter dash line, the mononuclear count with the fluid kept at the same temperature.

If the multilobed cells are of hematogenous origin, they may undergo autolysis from their self-contained protease. Autolytic digestion in leukocytes has been observed under many conditions. This autolysis, which may occur anywhere outside the blood stream, may be hastened

10. Levinson, A.: Cerebrospinal Fluid in Health and Disease, ed. 2, St. Louis, C. V. Mosby Company, 1923, p. 165.

by changes in the physical or chemical properties of the spinal fluid. This activity seems to be accelerated in normal fluids. No proteolytic enzymes have been demonstrated in spinal fluids other than those contained within the cells themselves. It is conceivable that as the autodigestive processes continue and cells are broken up, proteolytic enzymes may in some manner pass into the fluid, and the fluid may then have a proteolytic activity.

In hemorrhage into the spinal fluid, Bigelow [3] has pointed out the destructive action of the spinal fluid against the polymorphonuclear cells in particular, and likewise the relative resistance of the lymphocytes to this action.

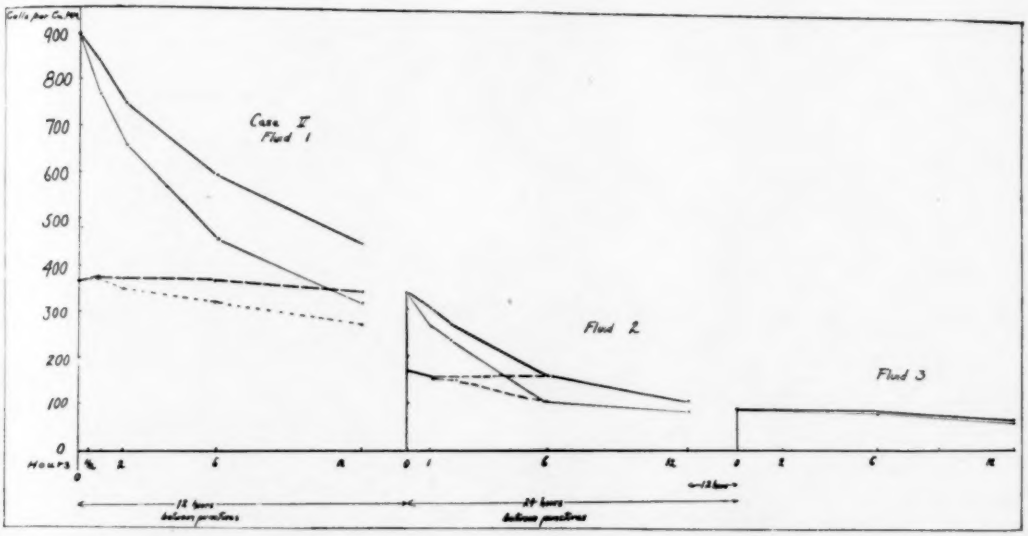

Chart 3.—The cytolytic action of spinal fluid in acute poliomyelitis. The dark continuous line represents the total cell count with the fluid kept at room temperature, 15 to 30 C.; the dark dash line, the mononuclear count with the fluid kept at the same temperature; the lighter continuous line represents the total cell count with the fluid kept in an incubator at 38 C.; the lighter dash line, the mononuclear count with the fluid kept in an incubator at the same temperature.

It hardly seems justifiable to compare cytolysis occurring in normal fluids into which a hemorrhage has occurred with that of fluids from a case of acute poliomyelitis. I am not certain that the multilobed cells are the same as the polymorphonuclear leukocytes of the blood. I do not know what changes in the fluid or in the cells may have been effected by the presence, or the passage through, of the virus in the case of the poliomyelitic fluid. This factor is not present in simple hemorrhagic fluid.

It is furthermore doubtful whether washed leukocytes taken directly from the blood and exposed to poliomyelitic spinal fluid would give a condition in which the cytolytic action of the spinal fluid could be fairly tested, even if one felt with Levinson that the multilobed cells were identical with the polymorphonuclear cells from the blood. The changes in environment produced by the citrate solution and physiologic sodium chloride solution would probably render this experiment unsatisfactory, even though the anatomic identity of the cells seemed unchanged. As can easily be shown, a cell as fragile as a polymorphonuclear leukocyte must have a minimum of physical and chemical irritation to be suitable for study in such a problem.

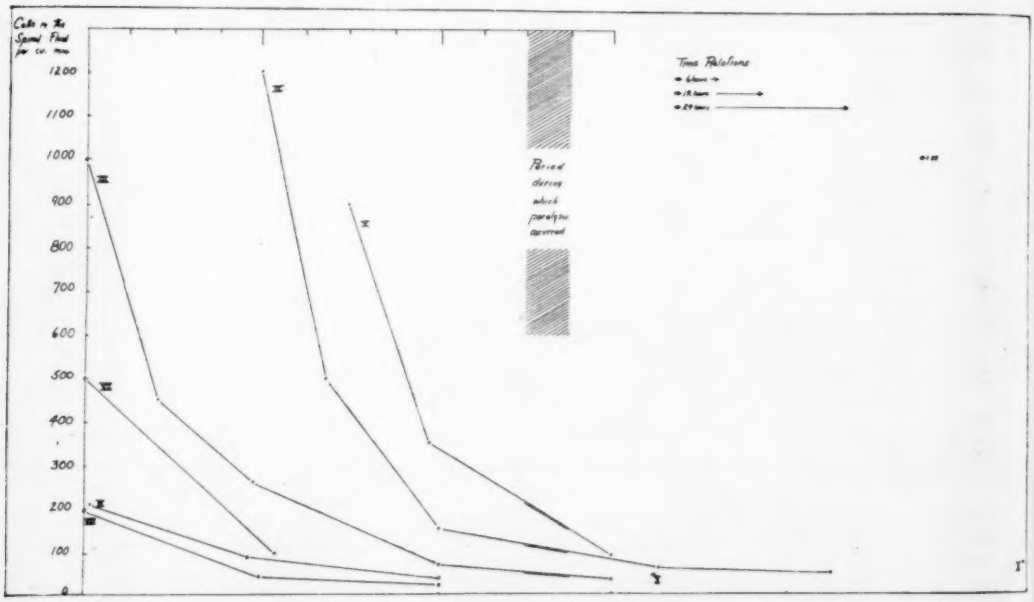

Chart 4.—Immediate or "bedside" cell counts in each case and its relation to the onset of paralysis in a series of eight cases. The Roman numerals refer to the individual case numbers; the curves, to the cell count changes in individual cases.

That physicochemical factors may be active as well as chemical cannot be denied. Levinson [11] reported that fluids in cotton-stoppered or opened tubes show a quick fall in the hydrogen ion concentration, falling quickly from p_H 7.4 to p_H 8.4. This is avoided, as in the present series, by stoppering the tubes tightly immediately after puncture. He has also shown that the fall in hydrogen ion concentration occurs because of the absorption of carbon dioxide from the air.

11. Levinson, A.: Cerebrospinal Fluid in Health and Disease, ed. 2, St. Louis, C. V. Mosby Company, 1923, p. 113.

The alkaline reserve of nonmeningitic fluids is given by Levinson [12] as averaging between 55 and 57 per cent of carbon dioxide bound by the cerebrospinal fluid at 0 C. and at a barometric pressure of 760 mm. of mercury. Under the same conditions, he has reported a poliomyelitic fluid as having an alkaline reserve of 45.7 per cent, while that of one of meningismus is given as 47.5 per cent. All other nonmeningitic fluids had a reserve above 55.7 per cent except that in a case of uremic coma, which showed 52 per cent of bound carbon dioxide.

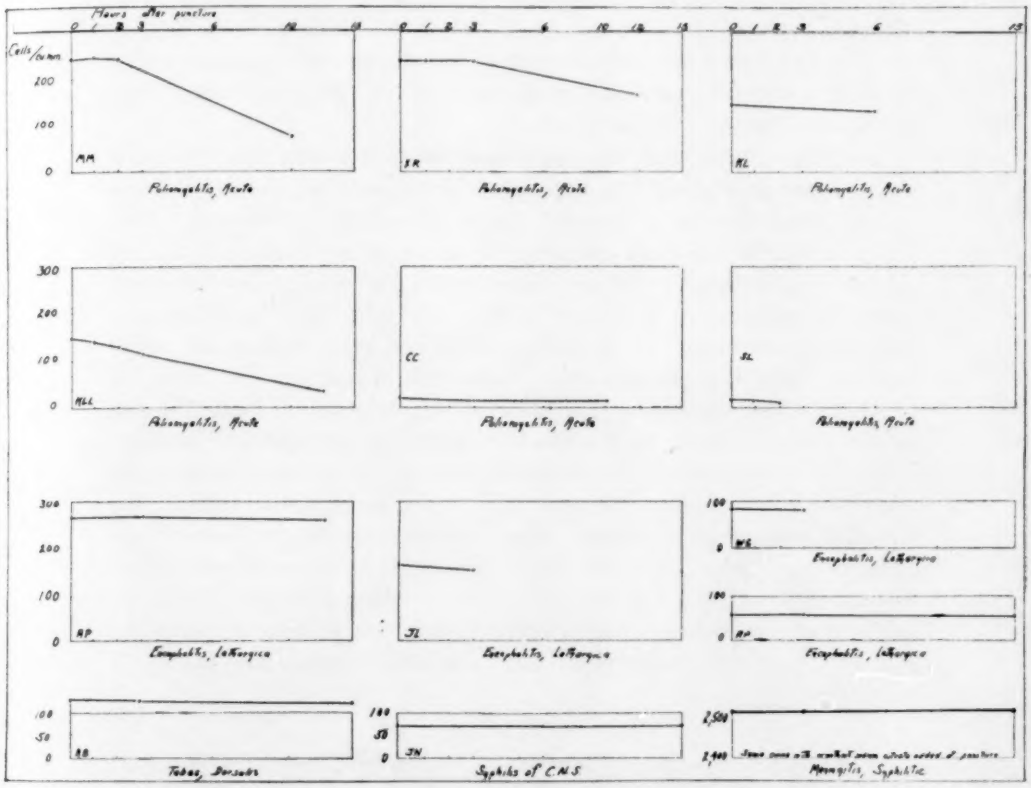

Chart 5.—Small cell counts reported by Wynn appearing in the *Journal of Laboratory and Clinical Medicine*, 1922, vol. 7, p. 273, and charted by the author.

The change of hydrogen ion concentration or alkaline reserve might in itself accelerate cytolysis. In the present series, however, it is doubtful whether there were any great changes in either of these factors, as the tubes were tightly stoppered with corks from the beginning, except when fluids were being withdrawn for examination. In spinal fluids

12. Levinson, A.: Cerebrospinal Fluid in Health and Disease, ed. 2, St. Louis, C. V. Mosby Company, 1923, p. 118.

that cannot be examined immediately, Levinson [13] has advocated the addition of 3 drops of dilute acetic acid to every 5 cc. of spinal fluid as a means of preserving the cellular elements for counting purposes. Morabito [4] stated that a few drops of glacial acetic acid added to the spinal fluid at the time of puncture will prevent cytolysis.

The surface tension of the spinal fluid may be another important factor that may affect the rate of cytolysis. It also may vary in disease, and it may change when the fluid is allowed to stand. It may be an important factor in the acceleration or inhibition of the other factors affecting cytolysis.

The fact that cytolysis occurs more rapidly in the incubator argues strongly for the chemical nature of the activity. Morabito [4] stated that cytolysis is inhibited in the icebox.

In view of the fact that so many physicochemical and chemical changes may take place, it is not easy to determine the exact mechanism of cytolysis in the fluids observed. It is not easy to ascribe such activities to a specific cytolysin occurring in poliomyelitic fluids only, for as yet there is no norm to be used as a standard of comparison; furthermore, the presence of multilobed cells in the spinal fluid is distinctly a pathologic condition. If there is a cytolysin characteristic of poliomyelitic fluids, it is probable that it does not appear until the time of, or shortly after, the shower of virus into the cerebrospinal fluid. Further studies must be made to disclose the nature of this cytolytic activity. It would be beyond the scope of this report to do more than make record of these observations and make brief mention of some of the chemical and physicochemical factors which may be involved in the changes observed. There are many difficulties to be overcome before this cytolytic activity can be understood. Suffice it to say, therefore, that one may encounter a high degree of cytolysis in those poliomyelitic spinal fluids which contain many cells, particularly when they are of the multilobed type.

CONCLUSION

1. Cytolysis has been observed in the early pleocytoses of acute poliomyelitis, which is more active toward the multilobed elements than toward the mononuclear elements.

2. Proof is given of the advisability of making spinal fluid cell counts immediately after lumbar puncture in all cases in which there may be a possibility of poliomyelitis.

3. A pleocytosis consisting of 50 per cent or more of multilobed cells, occurring in a clear fluid, is suggestive of acute poliomyelitic

13. Levinson, A.: Cerebrospinal Fluid in Health and Disease, ed. 2, St. Louis, C. V. Mosby Company, 1923, p. 194.

infection. When in the course of from twenty-four to thirty-six hours or so, the lumbar puncture is repeated and there is a fall in the total cell count with a shifting of the differential count to a mononucleosis of 90 per cent or more, one may be certain that the condition is one of poliomyelitic infection. This cellular response is pathognomonic, as it has not been observed in the spinal fluid in other conditions.

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ISO-AGGLUTININS IN THE NEW-BORN

WITH SPECIAL REFERENCE TO THEIR PLACENTAL TRANSMISSION *

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NEW YORK

It was demonstrated by von Decastello and Sturli,[1] Happ [2] and others that at birth the blood group of the infant is rarely established. Normally, the agglutinogens appear before the iso-agglutinins and by the end of the first year the blood grouping is usually complete.

The presence of iso-agglutinins in the blood from the umbilical cord raises the question as to their origin, whether they are a product of the biologic activity of the fetus or whether they have been transmitted from the mother by way of the placenta. If the iso-agglutinins find their source in the maternal circulation, observations as to their fate in the blood of the new-born would prove of interest. This consideration involves not alone the problem of placental permeability but the relationship of iso-agglutinins of the cord blood to the later development of blood groups by the infant.

HISTORICAL REVIEW

What constitutes the stimulus for the development of the elements in blood grouping is a matter of conjecture. Deluca [3] suggested that breast milk may convey these substances to the infant. This conception does not seem plausible, for although the breast milk of the mother contains the same receptors and iso-agglutinins as her own blood, still her blood may differ from that of her infant. Furthermore, Happ [2] did not find more iso-agglutinin in the blood of the nursing infant than in the one artificially fed.

Halban [4] early described the deficiency of the umbilical blood in iso-agglutinins and noted that at times the mother's serum was able to agglutinate the infant's blood. More rarely the mother's cells were

* Received for publication, Jan. 30, 1928.

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1. Von Decastello, A., and Sturli, A.: Ueber die Isoagglutinine im Serum gesunder und kranker Menschen, München. med. Wchnschr. **49**:1090, 1902.

2. Happ, W. M.: Appearance of Isoagglutinins in Infants and Children, J. Exper. Med. **31**:313, 1920.

3. Deluca F. A.: Contribution à l'étude des hémo-agglutinines en obstetrique, Rev. franç. de gynéc. et d'obstét. **20**:331 (May) 1925.

4. Halban, J.: Agglutinationsversuche mit mütterlichen und kinderlichen Blute, Wien. klin. Wchnschr. **13**:545 (June) 1900.

agglutinated by the cord blood. These observations, together with differences of an immunologic and chemical nature, led Halban to believe that the fetal blood was not totally dependent on the mother's blood and could be distinct from it in many respects. Halban and Landsteiner,[5] in comparing mother's serum from the retroplacental flow with serum from the umbilical cord, found quantitative differences between them as regards hemolytic activity for rabbit's cells, the infant possessing these hemolysins in much weaker concentration than the mother. Langer [6] observed that whereas the red cells of the new-born are as agglutinable as those of older children, their serum differed from that of the mother in being poor in iso-agglutinins.

These observations led to a discussion of the permeability of the placenta not alone to iso-agglutinins but to antibodies in general. In this field, a mass of conflicting evidence has accumulated. Schumacher,[7] working with typhoid agglutinins, and Polano [8] with diphtheria antitoxin, affirm their placental transmission, while the observations of Fellenberg and Döll,[9] who used a variety of bacterial agglutinins, do not support their views. Bourquin [10] studied this problem by active and passive immunization of pregnant guinea-pigs and rabbits and later by testing the fetal serum for the respective antibodies. She injected diphtheria antitoxin into the mother and traced its passage into the fetus. Also, by reversing these conditions, that is, by injecting the fetus, she was able to recover this antitoxin from the mother. Her results fully justified the conclusion that the placentas of these animals were permeable to antibodies. Kuttner and Ratner [11] confirmed the passage of diphtheria antitoxin through the human placenta, and attempted to reconcile the discordant results of observers on the basis of structural differences in the placentas of the various animal species used experimentally. From the anatomic studies of Grosser,[12] they pointed out that in the human placenta only a

5. Halban, J., and Landsteiner, K.: Ueber unterschiede des fëtalen und mütterlichen Blutserums und über eine agglutinations-und fällungs-hemmende Wirkung des Normalserums, München. med. Wchnschr. **49**:473 (March) 1902.

6. Langer, J.: Ueber Isoagglutinine beim Menschen, mit besonderer Berücksichtigung des Kindesalters, Ztschr. f. Heilk. **4**:111, 1903.

7. Schumacher, H.: Beitrag zur Frage des Ueberganges der im Serum gesunder und typhuskranker Wöchnerinnen enthaltenen Agglutinine auf den kindlichen Organismus, Ztschr. f. Hyg. u. Infectionskrankh. **37**:323, 1901.

8. Polano, O.: Der Antitoxin übergang von der Mutter auf das Kind, Ztschr. f. Geburtsh. u. Gynak. **53**:456, 1904.

9. Fellenberg, R., and Döll, A.: Ueber die biologischen Beziehungen zwischen Mutter und Kind, Ztschr. f. Geburtsh. u. Gynak. **75**:285, 1913.

10. Bourquin, H.: A Study on the Permeability of the Placenta, Am. J. Physiol. **59**:122, 1921.

11. Kuttner, A., and Ratner, B.: Importance of Colostrum to the New-Born Infant, Am. J. Dis. Child. **25**:413 (June) 1923.

12. Grosser, quoted by Kuttner and Ratner (footnote 11).

single layer of cells separates the maternal from the fetal blood, in which respect it is similar to that of rabbits, guinea-pigs and mice. In this group, then, the placental transmission of antibodies is more easily effected than in the type of animal such as the ruminant, who is provided with a complex placental structure.

Hirszfeld and Zborowski [13] stated that antibodies are not usually present in the blood of newly born animals, and that when antibodies are found in the blood from the umbilical cord they are probably derived from the mother. They asserted that the human placenta has a selective permeability for iso-agglutinins which varies with each of the four blood groups, the antibodies reaching the blood stream of the fetus most often when the mother and infant belong to group O. Also in the heterospecific pregnancy, when the mother and infant are of different blood groups, there is a tendency for the iso-agglutinins capable of affecting the infant's cells to disappear from the blood of the mother. These observations were not confirmed by Collon,[14] who did not observe this protective mechanism and who maintains, on the other hand, that the fetus is capable of elaborating its own iso-antibodies. Lazarewicz and Zborowski [15] ascribed this disagreement to differences in technic and to the use by Collon of maternal venous blood instead of retroplacental blood as used by Hirszfeld. Recently two Japanese workers, Hara and Wakao [16] found iso-agglutinins in 50 per cent of the cases in which blood from the umbilical cord was examined. The early disappearance of these iso-agglutinins suggested to them probable transmission from the mother. In fifteen samples of blood from the cord, Happ [2] could not detect iso-agglutinins.

My object in this paper is to present the results of an investigation undertaken to study the development of iso-agglutinins in the infant, with emphasis on the period from birth to ten days after birth. The question of placental permeability will also be considered, as the mother's contribution to the iso-agglutinins of her offspring is still a subject of controversy.

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13. Hirszfeld, L., and Zborowski, H.: Gruppenspezifische Beziehungen zwischen Mutter und Frucht und elektive Durchlässigkeit der Placenta, Klin. Wchnschr. **4**:1152 (June 11) 1925; Sur la perméabilité elective du placenta en rapport avec le groupe sanguin de la mère et du fetus, Compt. rend. Soc. de biol. **92**:1253 (March) 1925; Sur la symbiose serologique entre la mère et la foetus, ibid. **94**:205 (Jan. 29) 1926.

14. Collon, N. G.: Les isoagglutinines chez la mère et l'enfant, Compt. rend. Soc. de biol. **96**:144 (Jan. 21) 1927.

15. Lazarewicz, M., and Zborowski, H.: Sur la perméabilité du placenta pour les iso-agglutinines, Compt. rend. Soc. de biol. **95**:1213, 1926.

16. Hara, M., and Wakao, R.: Isohämoagglutination beim Kinde und in der Frauenmilch, Jahrb. f. Kinderh. **114**:313, 1926.

The general plan was to study the blood group factors at birth and at various periods during the first year. The first determinations were made at birth from the blood of the umbilical cord, the second at seven to ten days, prior to the infant's discharge from the hospital and finally when the infant was about 6 months old. When the opportunity presented itself, especially in doubtful cases, blood specimens were examined several times during the first year. Blood from the mother was also tested for agglutinogens and iso-agglutinins as soon after delivery as was possible, and also at the second period (at from seven to ten days after delivery), blood in both instances being withdrawn from the vein of the arm. The strength of the iso-agglutinins in the infant's serum was determined by titration at each test. Data were also included to determine any possible relationship between the severity of labor and placental permeability. Whether or not the appearance of icterus neonatorum is influenced by dissimilarity of blood groups between mother and child will be discussed in another paper.

TECHNIC

The blood obtained from the umbilical cord and from the vein of the mother was centrifugalized for serum, a few drops of the cells being first withdrawn into a tube containing 1.5 per cent sodium citrate in 0.85 per cent sodium chloride. After being washed twice in physiologic sodium chloride solution, the cells were made up to a 3 per cent suspension. During the later periods, blood from the infant was obtained by puncture from the heel, a small quantity being drawn up in a Wright capsule for serum and at the same time a few drops being collected in the citrate solution for cells. The serum and cells were treated in the same manner as the first samples.

To determine the presence of iso-agglutinins in the serums of the infants and mothers studied, they were tested against known adult group A and B cells (table 2). Similarly, group A and B serums stored in sealed tubes and kept on ice were employed to ascertain the existence of the agglutinogens. Whenever possible, the cells of the same group A and B persons were used in all of the tests conducted with the serum of a single patient. The necessity for keeping these cell suspensions fresh was emphasized when it was observed that older cells either did not agglutinate or were clumped too readily. Again, when the mixture of the infant's serum and the known group A and B cells did not produce agglutination, other persons of the same blood groups were used. This procedure was followed when the agglutination was questionable and always when iso-agglutinins evident in previous tests were absent from subsequent examinations.

Before each set of experiments, the agglutinability of the known group A and B cells was checked against stock A and B serums, by the open slide method. Observations were made with the naked eye and, when in doubt, with the microscope to eliminate the presence of any pseudo-agglutination due to deteriorated serum or cells or to some other less perceptible factor. For the actual tests, tubes with a diameter of 1 cm. and a length of 7 cm. were employed and were thoroughly cleansed and dried in the oven. A drop each of serum, physiologic sodium chloride solution and of 3 per cent suspension of cells were placed together

in a tube, according to the plan described by Landsteiner and Witt.[17] The tubes were shaken to secure thorough admixture, plugged with cotton and exposed for one hour to room temperature, which ranged between 20 and 25 C. A drop was then removed from each tube with a glass rod, placed on a slide and examined microscopically for agglutination. Subsequently the tubes were placed in the icebox, kept there over-night and the readings repeated as before. The tubes showing agglutination were then allowed to stand at room temperature for an hour and in questionable cases were exposed to incubator temperature, a procedure adopted to detect the presence of "cold" agglutinins; i. e., those acting only at low temperatures. According to the strength of the agglutination reaction, readings were recorded in each test as ranging from + to ++++, those that were doubtful and irregular as ∓, cognizance being taken of the latter in view of the possible development of "cold" or true iso-agglutinins in later experiments.

A typical experiment with a new-born infant taken at birth usually comprised sixteen tests, as shown in table 1.

When iso-agglutinins were absent in tubes 12 and 14, still larger quantities of serum were used. With a ratio higher than nine drops of serum to one of cells, results were not as sharply defined as those with the lower ratios. On the

TABLE 1.—*Protocol of a Typical Case*

Red Blood Cells	Serum				
	Group A	Group B	Infant's	Mother's	Saline
Infant's	1	2	3	4	5
Mother's	6	7	8	9	10
Group A	*	*	11 12	15	
Group B	*	*	13 14	16	

* These tests were carried out on slides. The numbers designate the tubes. All tubes contain one drop each of cells, serum and saline solution except tubes 8, 12 and 14, which for the purposes of titration do not contain saline but four drops of infant's serum and one drop of cells. Tubes 5 and 10 do not contain serum and serve as cell controls.

seventh to the tenth day (second period) and again at later intervals during the first year, not all of the 16 tubes were set up, but those were included which had for their purpose a regrouping of the cells (tubes 1 and 2) and the titration of the agglutinins (tubes 11, 12, 13 and 14) to determine whether there had been any diminution or increase in iso-agglutinin content compared with determinations at birth. In the second and subsequent periods the amount of serum available was limited, but whenever possible complete titration was carried out, a procedure of particular importance in those instances in which the infant's iso-agglutinins that had once been present had disappeared. Control experiments of cells with serum and with saline solution (tubes 3 and 5) were carried out, and when a difference of blood groups existed between mother and infant, cross agglutination tests were also included (tubes 4 and 8). When an isohemolysin was encountered, a few drops of the infant's serum were exposed to a temperature of 56 C. to destroy the complement so as not to mask the accompanying agglutination. The isohemolysins "α" and "β" were recorded in a similar fashion to the agglutinins.

In this paper the newer terminology has been used, the two pairs of blood qualities, A, B, α, β being adhered to. To facilitate the analysis of these studies, the blood groups may be represented as shown in table 2.

17. Landsteiner, K., and Witt, D. H.: Observations on the Human Blood Groups, J. Immunol. **11**:221 (March) 1926.

BLOOD GROUP FACTORS IN THE INFANT

The Development of the Blood Group Factors in the Infant.—In seventy-one of the seventy-five cases in this series, the cord blood was available for examination. The results are summarized in table 3.

Of those whose cord serum had been examined, fifty-seven were followed in the outpatient department. In these the iso-agglutinins and agglutinogens were tested at various times during the first year of life.

TABLE 2.—*Newer Terminology for Blood Groups*

Group	Red Blood Cells	Serum
O (I)*	Do not possess agglutinogen and therefore are not agglutinable by any serum	Agglutinins "α" and "β" present; agglutinates cells of groups A, B and AB
A (II)	Possess agglutinogen "A". Agglutinated by serum of groups O and B	Agglutinin "β" present; agglutinates cells of groups B and AB
B (III)	Possess agglutinogen "B". Agglutinated by the serum of groups O and A	Agglutinin "α" present; agglutinates the cells of groups A and AB
AB (IV)	Possess agglutinogens "A" and "B"; agglutinated by the serum of groups O, A and B	No iso-agglutinins present; can not agglutinate cells of any group

* The letters refer to a more simplified method of designating the blood groups in that they substitute for the usual Jansky numbers (in parenthesis) the agglutinogen present in each (New Designations for Blood Groups, editorial, J. A. M. A. **88**:1421 [April 30] 1927). In preparing this chart, consideration has not been given to the subdivision of blood groups through the discovery of extra factors.

TABLE 3.—*Analysis of Cord Blood with Reference to the Incidence of Agglutinogens, Iso-Agglutinins and Complete Blood Groups*

	Total Cases	Percentage
Cord blood examined	71	
Agglutinogens present of groups A, B and AB	33	
Iso-agglutinins and agglutinogens of groups A and B appearing together in cord blood	15	
Instances in which "α" iso-agglutinin occurred alone in the cord blood	3	
Instances in which "β" iso-agglutinin occurred alone in the cord blood	4	
Instances in which "α" and "β" occurred together in cord blood	19	
Total number of specimens of cord blood containing iso-agglutinins	41	
Percentage of specimens of cord blood containing iso-agglutinins	..	57.7
Instances in which cells and serum of cord blood allowed for complete blood grouping	35	
Percentage of complete blood groups in cord blood	..	49.2

Unfortunately, it was not always possible to obtain more than one specimen following the one taken at ten days, so that a statement cannot be made with any degree of accuracy as to the exact time when the individual factors made their appearance. Of the fifty-seven, complete blood groups were established at birth in twenty-seven. As will be described later, the iso-agglutinins that partake in this blood grouping undergo changes, so that at the ten day period this number becomes smaller. Of the thirty remaining, all but one possessed their full quota of blood group components within one year. One was not examined until thirteen months later, when the blood group was complete.

As shown in table 3, the cord blood of thirty-five new-born infants fell into one of the four adult blood groups, as judged by the interaction of infant's cells with known serum and group A and B cells with cord serum. The incidence of complete blood groups stated by various workers doubtless depends in large part on the detailed procedure followed in the determinations. Thus Happ [2] examined fifteen specimens of cord blood and was unable to detect iso-agglutinins in any of them, although one infant belonged to group AB and possessed both receptors. He employed hanging drop suspensions of one drop each of known cells and cord blood serum. Jones,[18] on the other hand, was able definitely to group 78.8 per cent of 197 specimens of blood from new-born infants. His method involved the use of flat slide preparations and about 10 to 12 parts of the fetal serum to one of cells. In the present investigation it was noted that with the use of larger amounts of serum (nine parts or more of serum to one of cells), the readings were difficult to make and that the most sharply defined reactions were obtained with the more

TABLE 4.—*Analysis of the Changes in Iso-Agglutinin Content during the First Ten Days of Life*

	Total Cases	Percentage
Iso-agglutins in cord serum	41	
Reexamined within ten days	36	
Decrease in titer	13	36.1
Total disappearance of iso-agglutinins	14	38.8
Total number with decrease or loss of iso-agglutinins	27	65.8
Increase in titer	3	8.3
Titer unchanged	6	16.6
Iso-agglutinins appearing for the first time within ten days	4	

concentrated mixtures. It was also observed that when the tests were carried out on flat slides, exposure to air for any considerable length of time was followed by questionable results.

Diminution in Concentration of Iso-agglutinins during the First Ten Days after Birth—Reference is made in table 4 to the fluctuations in iso-agglutinin strength during the first ten days of postembryonic life. In twenty-seven of the forty-one cases in which iso-agglutinins were definitely detected in the blood from the umbilical cord, reexamination within ten days revealed either a diminution in their titer or their complete disappearance. In table 5 is presented a summary of fifteen cases of this important group in which the iso-agglutinin content of the cord serum is compared with the serum ten days after birth, illustrating in the main the loss of iso-agglutinin strength following birth. In five cases not included in this table, four showed a decrease in titer after the tenth day, and in another in which the first specimen was obtained on the fifth day the iso-agglutinin then observed was no

18. Jones, B. B.: Iso-Agglutinins in the Blood of the New-Born, Am. J. Dis. Child. **22**:586 (Dec.) 1921.

TABLE 5.—*Analysis of the Concentration of Iso-Agglutinins in the Cord Blood as Compared with the Later Periods of Infancy* *

	Mother's Blood Grouping			Infant's Blood									
				Cord Blood		Second Specimen		Later Specimens During the First Year				Final Blood Group of the Infant	
Infant	Cells	Serum	Group	Cells	Serum	Cells	Serum	Cells	Serum	Cells	Serum	Cells	Serum	Group
M. L.	B	α	B	O	α ++ β, abs.	10 days O	α, abs. β, abs.	6 months O	α ++ β ++	..	.....	O	α β	O
J. C.	O	α β (also hem. β)	O	O	α, abs. β ++ (also hem. β)	14 days O	α, abs. β, abs.	1 year O	α +++ β +++	..	.....	O	α β	O
R. W.	O	α β	O	B	α ++ β, abs.	10 days B	α, abs. β, abs.	8½ months B	α +++	..	.....	B	α	B
J. S.	O	α β	O	O	α +++ β ++	11 days O	α + β, abs.	5½ months O	α ++ β ++	..	.....	O	α β	O
R. F.	O	α β (also hem. α)	O	O	α ++ β +++ (also hem. β)	11 days O	α ++ β + (also trace of hem. β)	6 months O	α + β, abs.	6½ months O 9 months O	α +++ β, abs. α +++ β ++	O	α β	O
H. R.	O	α β	O	O	α ++ β ++ (also hem. β)	10 days O	α ++ β, abs.	8 months O	α ++ β ++	..	.....	O	α β	O
W.DeV.	O	α β (also hem. α)	O	O	α ++ β ++ (also hem. α and β)	10 days O	α + β +	6½ months O	α ++ β, abs.					
R. B.	A	β	A	A	α, abs. β ++	10 days A	α, abs. β, abs.	7 months A	α, abs. β +	..	.....	A	β	A
D. C.	A	β	A	A	α, abs. β +	11 days A	α, abs. β, abs.	7 months A	α, abs. β +++	..	.....	A	β	A
S. C.	O	α β	O	O	α +++ β +	10 days O	α + β, abs.	7 months O	α +++ β +++	..	.....	O	α β	O
T. C.	O	α β	O	O	α ++ β ++	16 days O	α, abs. β, abs.	5½ months O	α, abs. β ++	9½ months O	α +++ β +++	O	α β	O
M. C.	O	α β (also hem. α and β)	O	O	α, † marked hem. β +++ (also hemolysis)	15 days O	α ++ β ++ (also hem. α and β)	9 weeks O	α ++ β, abs. (no hem.)	1 year O	α +++ β ++	O	α β	O
A. F.	O	α β	O	O	α ++ β, abs.	9 days O	α, abs. β, abs.	13 months O	α +++ β +++	..	.....	O	α β	O
V. H.	O	α β	O	O	α +++ (also marked hemolysis) β † (marked hemolysis)	9 days O	α and β† (marked hemolysis)	4 months O	α + β +++	9 months O	α +++ β +++ (also hem., α and β)	O	α β	O
C. M.	A	β	A	O	α, abs. β ++	10 days O	α, abs. β, abs.	10 months O	α +++ β ++					

* To simplify this table and table 7, the results obtained from the various individual titrations have been consolidated, the following symbols being used in their stead: 0, no receptors; abs., no iso-agglutinins; +, slight but definite agglutination; ++, moderate, and +++, marked agglutination; hem., hemolysin.

† In these cases there was not sufficient serum to repeat the tests after heating so as to obviate the effect of the hemolysin. The degree of hemolysis in these instances must, therefore, serve as an index of accompanying iso-agglutination.

longer in evidence on the tenth day. Two cases will be discussed under another heading that also present the characteristic features of this group.

The Similarity between the Iso-agglutinins of the New-Born and of the Mother.—In table 6 those cases have been compiled in which the blood group of the mother differs from the final group of the infant. By comparing the nature of the iso-agglutinins in parent and cord blood, results are available which have an obvious bearing on the problem of the placental transmission of iso-agglutinins. Examination of the table brings out the striking parallelism between mother and new-born concerning iso-agglutinins. With a mother in group O the new-born may,

TABLE 6.—*Analysis of the Iso-Agglutinins in Maternal and Cord Blood*

	Blood Group of Mother			Iso-agglutinins in	Final Blood Group of Infant		
Infant	Cells	Serum	Group	Cord Blood	Cells	Serum	Group
1. J. M.	O	α and β	O	β	A	β	A
2. V. S.	..	Same	O	β	A	β	A
3. P. F.	..	Same	O	β	A	β	A
4. J. B.	..	Same	O	β	A	β	A
5. M. H.	..	Same	O	β	A	β	A
6. R. W.	..	Same	O	α	B	α	B
7. V. M.	..	Same	O	α	B	α	B
8. E. W.	..	Same	O	α	B	α	B
9. J. W.	..	Same	O	α	B	α	B
10. C. M.	A	β	A	β	O	α and β	O
11. G. F.	..	Same	A	α and β absent	O	α and β	O
12. W. McN.	..	Same	A	α and β absent	O	α and β	O
13. J. D.	..	Same	A	α and β absent	O	α and β	O
14. J. V.	..	Same	A	α and β absent	O	α and β	O
15. K. O'C.	..	Same	A	α and β absent	O	α and β	O
16. M. L.	B	α	B	α	O	α and β	O
17. A. C.	B	α	B	α and β absent	A and B	α and β absent	AB
18. M. D.	A and B	α and β absent	AB	α and β absent	A	β	A
19. A. A.	A and B	α and β absent	AB	α and β absent	A	β	A

of course, possess one or both iso-agglutinins without throwing any light on their source. When the mother is, however, in group A or B, in which only one iso-agglutinin is present, the study of the fetal blood becomes more significant. In these cases it is observed that either iso-agglutinins are not detected in the cord serum or β or α is demonstrated, respectively, representing the same blood qualities as the mother's. Later, the infant may acquire the remaining iso-agglutinin, completing the requisites of group O, or the agglutinogen appears, placing the infant in the same blood group as the mother. In two cases in which the mother belonged to group AB, the cord serum was devoid of iso-agglutinins also. In one of these (case 18), 15 drops of cord serum were used in the reaction. Taken together with the diminution in iso-agglutinin concentration during the week or ten days following

birth, the evidence is strongly suggestive of the passive transfer of maternal iso-agglutinins into the fetal circulation.

Cases Illustrating Apparent Change of Blood Grouping during First Ten Days of Life and Further Confirming the Placental Transfer of Iso-agglutinins.—As these studies progressed and the cases showing a decrease in iso-agglutinin titer multiplied, it was regarded as highly probable that one or both of the iso-agglutinins derived from the mother might be permanently lost shortly after birth. With the later acquisition of an agglutinogen it would appear on comparing the cord blood with later specimens that the infant's blood group had undergone a change. Two such examples were encountered in this series.

CASE 1.—F. D., a boy, weighed 6 pounds and 3 ounces (2,812.6 Gm.) at birth; the delivery was normal. The mother's blood belonged to group O. The cord blood contained a trace of "α" iso-agglutinin and a moderate amount of "β," and as the red cells were inagglutinable, the infant also belonged to group O. Ten days later the mother's blood still belonged to group O, whereas the infant had lost both of its iso-agglutinins. The blood specimen showed, however, at this time the presence of "A" agglutinogen. When the infant was 10 weeks old, the blood again showed the "A" receptor and also a trace of "β" iso-agglutinin. At 8 months, the "β" iso-agglutinin was marked. With the acquisition of the "A" receptor and the reappearance of the "β" iso-agglutinin, the infant's blood could definitely be placed in group A. The source of the "A" receptor was the father whose blood belonged to group A.

CASE 2.—C. H., a boy, weighed 6 pounds and 12 ounces (3,067.7 Gm.) at birth; the delivery was normal. The mother's blood and that from the cord fell definitely into group O since each contained marked amounts of "α" and "β" iso-agglutinins and no receptors. When tests were again made seven days later, the mother was still in group O, while the infant's blood specimen no longer showed the existence of iso-agglutinins. The red cells had by this time acquired the "B" receptor. When the infant was 3 months of age, his serum showed the "B" receptor and a moderate amount of the "α" iso-agglutinin. At 8 months, there was a duplication of these changes in the infant's blood, namely, the "B" agglutinogen and a marked amount of the "α" iso-aglutinin. With the mother's blood as first observed in group O, the infant now belonged to group B.

Summarizing these important changes, it is evident that the mother's blood and the blood from the umbilical cord both contained the iso-agglutinins "α" and "β" and therefore fell into group O. Later with the loss of "α" in one case and "β" in the other and the further development of the "A" and "B" receptors, the infant's blood satisfied the requirements of groups A and B, respectively, while the blood of the mother, as would be expected, remained in the original group. It should be emphasized that the changes illustrated by these two cases are not at variance with the current conception concerning the immutability of blood groups. To repeat, the iso-agglutinins that had disappeared did not properly belong to the new-born but had probably been acquired from the mother by placental transmission.

Relation Between Changes in Iso-agglutinin Titer and Changes in Serum Protein Concentration.—It might be conceived that the tendency for iso-agglutinins to diminish is dependent on possible blood dilution during the ten-day period after birth. The percentage of serum protein was therefore determined in fifteen cases on both the cord blood and on specimens obtained from the infant at about ten days after birth, simultaneously carried out with tests for iso-agglutinins. The serum protein percentage was used, as this determination not alone measures the concentration of serum proteins but indicates the extent of plasma dilution. The Abbe dipping refractometer was employed, with the auxiliary prism for serum. With each determination on the serum, distilled water readings were likewise made. From the refractive index, the serum protein percentage was calculated according to the method outlined by Reiss.[19] Criticism of these calculations has been made of late owing to the fact that the serum albumin-globulin ratio which Reiss regarded as constant has been found to vary considerably. Neuhausen and Rioch [20] recently established what are probably more accurate factors for the nonprotein constituents and for serum protein that would tend to lower the values for serum protein percentage obtained heretofore, and make them adhere more closely to Kjeldhal determinations. For the purposes of the present investigation, in which simply the matter of relative differences of serum dilution was in question, the calculations according to the older method are entirely adequate.

As brought out in table 7, the cord blood was generally more concentrated than the specimens from the ten day period, though not universally so. The degree of decrease in iso-agglutinin titer when this occurred was not, however, commensurate with the serum dilution. In case 1, for instance, in which there was only a slight diminution in serum protein percentage, iso-agglutinin "β" present in moderate amount in the cord serum could no longer be demonstrated at ten days. Again in case 15, in which the serum was more concentrated at ten days than at birth, the iso-agglutinin "β" was markedly diminished, whereas the "α" remained the same. In case 2, there was only a slight lowering of serum protein, yet the "α" iso-agglutinin remained of the same strength while "β" could no longer be detected. Case 3 illustrates a similar discrepancy. If the dilution of the serum was responsible for changes in the titer of iso-agglutinins, it should, of course, affect each iso-agglutinin in like fashion. Table 7 shows in the main that the concentration of serum cannot be held accountable for changes in iso-agglutinin content.

19. Reiss, E.: Die refraktometrische Blutuntersuchung und ihre Ergebnisse für die Physiologie und Pathologie des Menschen, Ergebn. d. inn. Med. u. Kinderh. **10**:531, 1913.

20. Neuhausen, B. S., and Rioch, D. M.: The Refractometric Determination of Serum Proteins, J. Biol. Chem. **55**:353, 1923.

TABLE 7.—*The Relation between Serum Protein Percentage and the Concentration of Iso-Agglutinins*

	Infant's Blood					
	Cord Serum		Second Specimen		Later Specimens	
Infant	Serum Protein, per Cent	Iso-agglutinin	Serum Protein, per Cent	Iso-agglutinin	Serum Protein, per Cent	Iso-agglutinin
1. C. M.	6.97	α, abs. β ++	6.87	10 days α, abs. β, abs.	6.35	10 months α +++ β ++
2. H. R.	6.62	α ++ β ++	6.03	10 days α ++ β, abs.	7.80	8 months α ++ β ++
3. G. P.	7.95	α +++ β ++	6.82	10 days α ++ β ++	8.0	10 months α +++ β +++
4. J. S.	6.67	α +++ β ++	5.96	11 days α + β, abs.	6.86	5½ months α ++ β ++
5. J. M.	6.08	α, abs. β +++	6.05	10 days α, abs. β +		
6. M. L.	5.40	α, + β, abs.	5.53	10 days α, abs. β, abs.	6.62	6 months α ++ β ++
7. V. M.	7.18	α +++ β, abs.	6.8	10 days α ++ β, abs,	7.56	6 months α +++ β, abs.
8. J. D.	6.29	α, abs. β, abs.	6.13	10 days α, abs. β, abs.		
9. I. B.	6.08	α, abs. β, abs.	5.81	10 days α, abs. β, abs.		
10. E. C.	7.24	α + β, abs.	6.36	10 days α, abs. β +	8½ months 7.09 α ++ β, abs.	10½ months 7.22 α +++ β ++
11. A. C.*	6.37	α, abs. β, abs.	7.43	10 days α, abs. β, abs,	6.78	6 months α, abs. β, abs.
12. M. D.	5.36	α, abs. β, abs.	6.08	10 days α, abs. β ++	6.58	8 months α, abs. β +++
13. J. D.	5.85	α, abs. β, abs.	7.01	10 days α, abs. β, abs.	6.60	7 months α +++ β +++
14. E. O.	6.94	α, abs. β ++	5.94	11 days α, abs. β, abs.		
15. R. F.	6.98	α ++ β +++	7.50	11 days α ++ β +	9.84†	6 months α + β, abs.
					8.03	6½ months α +++ β, abs.
					8.15	9 months α +++ β ++

* The blood belonged to group IV, which does not possess any iso-agglutinins.

† The infant had a severe furunculosis at this time. She was well in the subsequent periods.

Holt and Reynolds [21] demonstrated that the hemagglutinating property of serum is contained in the pseudo-globulin fraction. Since the serum protein percentage does not furnish information regarding the component proteins, it cannot serve as an index of iso-agglutinin acquisition.

Relation of the Severity of Labor to Incidence of Iso-agglutinins in Cord Blood.—In order to determine whether difficult labor facilitates the passage of iso-agglutinins through the placenta, an analysis has been made of sixty-nine cases in which iso-agglutinins were present in the mother's blood (table 8). Only eighteen cases could be placed in the category of prolonged or abnormal labor. The incidence of iso-agglutinins in the cord serum in both groups was so much alike that significance could not be attached to the influence of this factor.

COMMENT

The results cited to a great extent bear out the views of Hirszfeld and his co-workers, namely, that the iso-agglutinins contrary to the

TABLE 8.—*Relation between the Type of Labor and the Occurrence of Iso-Agglutinins in Cord Serum*

	Total Cases	Percentage
Cases of difficult labor	18	
Iso-agglutinins absent from cord blood	7	38.9
Iso-agglutinins found in cord blood	11	61.1
Cases of normal labor	51	
Iso-agglutinins absent from cord blood	21	41.2
Iso-agglutinins found in cord blood	30	58.8

agglutinogens are not found except in the course of extra-uterine life, and when iso-agglutinins are present in the cord blood they have been transmitted from the mother. Whenever iso-agglutinins were found in the cord serum they never varied from those of the mother. In the two cases in which the mother's blood belonged to group AB (no iso-agglutinins), the cord serum was also devoid of iso-agglutinins. The decrease in titer and loss of iso-agglutinins soon after birth serves also as confirmatory evidence for this hypothesis. Hara and Wakao [16] came to the same conclusions after noting the close agreement between cord blood iso-agglutinins and those of the mother, with the disappearance of the former after birth.

On the other hand, this theory has its shortcomings. If the iso-agglutinins are transferred from the mother, it is difficult to understand why with a mother in group O ("α" and "β" iso-agglutinins) the cord serum frequently contains only one of the iso-agglutinins. An explanation for this circumstance may possibly be found in the recent work

21. Holt, R. L., and Reynolds, F. H. K.: The Hemagglutinating Fraction of Human Serums, J. A. M. A. **79**:1684 (Nov. 11) 1922.

of Kritschewski and Schwarzman [22] who, among others, showed that human tissues and organs have the capacity to absorb iso-agglutinins. It might be assumed that the placental tissues remove one of the iso-agglutinins in like manner.

Collon [23] illustrated his objections by cases in which the cord blood showed the evidences of iso-agglutinins different from those of the mother and contended, therefore, that the fetus is fully capable of producing its own iso-agglutinins. Although such instances were not encountered in this study, their occurrence is entirely probable. In the data presented (tables 5 and 6), there are examples of a mother in group A or B whose infant eventually was to be in group O. The cord blood of these patients, however, regularly either did not contain any iso-agglutinin or the one corresponding to the mother's, the second one to be acquired later.

Doubtless, the fetus can to a degree elaborate iso-agglutinins, but the foregoing results warrant the assumption that they may also originate in the maternal blood stream. The latter remain in the circulation of the infant for a short time to be replaced by iso-agglutinins of its own manufacture, in the majority of instances similar to the original. That an iso-agglutinin in the cord serum may be entirely lost, never to reappear, was shown in the two cases already described and confirms the view of placental transmission.

The passive transfer of iso-agglutinins from mother to fetus may be compared to the temporary increase in iso-agglutinin concentration in infant's blood after transfusions, as described by Bakwin, Astrowe and Rivkin.[24] It is also analogous to the transfer of diphtheria antitoxin from mother to child. Ruh and McClelland [25] considered that the correspondence between mother and infant as regards diphtheria antitoxin implies a direct transference of these immune bodies from mother to child by way of the placenta.

The two cases referred to in which iso-agglutinins disappeared and a receptor developed are important from the medicolegal standpoint. According to the generally accepted view, advanced originally by von Dungern and Hirschfeld [26] and since corroborated by large series of

22. Kritschewski, I. L., and Schwarzmann, L. A.: Die Gruppenspezifische Differenzierung der menschlichen Organe, Klin.Wchnschr. **6**:2081 (Oct. 29) 1927.

23. Collon, N. G.: Les anticorps dans le sang maternel et placentaire, Compt. rend. Soc. de biol. **94**:418, 1926.

24. Bakwin, H.; Astrowe, P. S., and Rivkin, H.: Transfused Blood in Infants with Severe Malnutrition, Am. J. Dis. Child. **33**:442 (March) 1927.

25. Ruh, H. C., and McClelland, J. E.: Camparison of Diphtheria Immunity in the Mother and in the New-Born, Am. J. Dis. Child. **25**:59 (Jan.) 1923.

26. Von Dungern, E., and Hirschfeld, L.: Ueber Vererbung gruppenspezifischer Strukturen des Blutes, Ztschr. f. Immunitätsforsch. u. exper. Therap. **6**:284, 1910.

cases, the receptor A or B can never appear in the blood of the infant if absent from that of both parents. The receptors may, however, be present in either or in both parents and may not appear in the child. In the two cases described, a receptor was not present in the cord blood, but both iso-agglutinins were in evidence, so that the group could be considered complete. As the infant was in group O, the legitimacy could not be questioned. With the dropping out of an iso-agglutinin and the development of an agglutinogen, the problem of parentage is reopened for consideration. The obvious means of avoiding this confusion would be to wait a reasonable time after birth before the blood group of the infant is employed to determine legitimacy. Other types of blood group changes, of course, occur through the natural acquisition of iso-agglutinins and agglutinogens during the first year of life. The permanent loss of an iso-agglutinin, once it has been acquired, has been questioned by Happ.[2]

The tardy development of iso-agglutinins and receptors has its practical application in relation to transfusion. Here it is well to stress the importance of preliminary blood grouping and compatibility tests in every case no matter how young the infant and even when the mother is to act as donor. This investigation also shows that it is impossible to foretell when the infant acquires its own iso-agglutinins. It is hazardous to rely on the low titer of iso-agglutinins in the infant's blood as compared with the adult donor for the safety of a transfusion. After one transfusion has been performed, it is wise to repeat these tests, particularly when the subsequent transfusions take place within the early days of infant life. One transfusion may stimulate the production of iso-agglutinins in the infant, or the final blood grouping may be independently established during this period.

SUMMARY AND CONCLUSIONS

The cord blood of seventy-one new-born infants was examined for iso-agglutinins and agglutinogens. In 49.2 per cent of these cases, the blood was equipped with its full quota of receptors and iso-agglutinins so that it could be placed in one of the four established blood groups. This percentage is increased during the first year by the later acquisition of these blood qualities.

In twenty-seven of forty-one cases in which iso-agglutinins were detected in the blood from the umbilical cord, reexamination within ten days revealed either a diminution in their titer or their complete disappearance.

There exists a close correspondence qualitatively between the iso-agglutinins of the cord and maternal blood, although the blood group may differ through the presence of a dissimilar agglutinogen.

In fifteen cases, the serum protein was determined from the cord blood and from the same infant at about ten days after birth, the iso-agglutinin titer being tested for at the same time. It was found that simple blood dilution could not be held responsible for the diminution in iso-agglutinin strength following birth.

The similarity that exists between the blood of the new-born and that of the mother with respect to iso-agglutinins, as well as the tendency of the latter to diminish in titer soon after birth, suggests their passive transfer from the maternal into the fetal circulation through the placenta. This process is analogous to the passage of diphtheria antitoxin from mother to child.

In two cases iso-agglutinins definitely demonstrated in the cord blood were absent from all subsequent examinations. In these instances, the iso-agglutinins lost were probably derived from the mother by placental transmission. With the later development of an agglutinogen and associated iso-agglutinin by the infant, its own blood group was established. In these cases, the cord blood possessed both iso-agglutinins and thus could be placed in group O, whereas the eventual blood groups as developed by the infant were A and B respectively. Such changes are probably not uncommon and have their forensic significance, as the iso-agglutination reaction is employed in establishing paternity. From this standpoint, it would seem appropriate to defer these tests for about two weeks after birth until the permanence of the iso-agglutinins is assured. These limitations apply especially to cases in which the cord blood belongs to group O.

The fluctuations in iso-agglutinin concentration in early infancy as well as the uncertainty as to the time when the various blood group factors are developed necessitates the repetition of blood group and compatibility tests preliminary to each transfusion in the young infant.

The severity of labor probably does not bear any influence on the passage of iso-agglutinins through the placenta.

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ICTERUS NEONATORUM

ITS RELATION TO THE COMPATIBILITY OF BLOOD GROUPS BETWEEN MOTHER AND NEW BORN *

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The isohemolytic reaction subsequent to the use of improperly matched blood in transfusions has the appearance of jaundice as one of its outstanding features. The reason for this complication probably lies in the sudden liberation of large amounts of hemoglobin. It has been suggested by Ottenberg [1] that icterus neonatorum might be explained on a similar basis; namely, that it is due to the accidental transfusion of incompatible blood between mother and fetus through an opening in the placenta. My object in this paper is to present data bearing on the possibility of the blood group of mother and fetus being related to the development of icterus neonatorum.

Icterus neonatorum is generally regarded as the manifestation of a physiologic bilirubinemia which occurs most commonly from the second to the eleventh day of postembryonic life. The statistics of its frequency depend in large part on the observer's interpretation of jaundice. Von Reuss [2] quotes a range of from 15 to 84 per cent, and if the faintest grades of icterus are included, it takes place in all new-born infants, according to Brechet.[3] In a recent study, Hilgenberg [4] noted its appearance in 68 per cent of 564 living infants.

Anyone who has observed a considerable number of new-born infants during the first days of life is familiar with the difficulties of determining the presence of icterus. The milder grades are often obscured by the normal pink hue of the skin, so that for purposes of this investigation, it is best to consider only those cases in which jaundice is unquestioned.

REVIEW OF THE LITERATURE

The numerous and contradictory conceptions of the origin of icterus neonatorum have been clearly summarized in a recent review by Van

* Received for publication, Jan. 30, 1928.

* From the Department of Pediatrics, Cornell University Medical College and the New York Nursery and Child's Hospital.

1. Ottenberg, R.: The Etiology of Eclampsia, J. A. M. A. **81**:295 (July 28) 1923.

2. Von Reuss, A. R.: Diseases of the New-Born, New York, William Wood & Company, 1922, p. 55.

3. Brechet: quoted by von Reuss (footnote 2, p. 57).

4. Hilgenberg, F. C.: Statistischer Beitrag zur Frage des Icterus neonatorum simplex, Monatschr. f. Geburtsh. u. Gynäk. **68**:326 (March) 1925.

Creveld.[5] Of the five groups established in his classification, the one bearing on the relationship of the destruction of the red cells in the circulation of the fetus and of the new-born infant to icterus calls forth the most ardent discussion. In view of the existing polycythemia at birth, to ascribe the icterus to the decrease in the number of red cells during the first days of life offers a most tempting hypothesis. The icteric and nonicteric infant have been compared with reference to red cell and platelet counts, to fragility of their red corpuscles, to coagulation time, to quantitative determinations of bile pigment in the feces and urine and to the iron content of the placenta, but with conflicting conclusions. Lepehne[6] and Andrewes[7] obtained only indirect van den Bergh reactions with the serum of icteric new-born infants, evidence apparently for the hemolytic and extrahepatic origin of bilirubin. Grulee and Mebane[8] found, however, that this test was not reliable in differentiating between obstructive and nonobstructive types of jaundice in infants and young children.

With the physiologic fall in the number of red blood corpuscles, Yllpö[9] would account for a coincident icterus on the basis of the inability of the functionally immature liver to take care of the biliary products formed. Hess[10] employed the duodenal catheter to aspirate the bile of new-born infants and concludes that the jaundice is due to a defective correlation between biliary excretion and secretion, the latter being dependent on an increased supply of available hemoglobin. Schick[11] believes that the blood pigment derived from the decomposition of maternal blood, particularly that of the intervillous spaces of the placenta, is the precursor of the bilirubin involved in icterus neonatorum and that the fetal iron is derived from the same source. Williamson[12] pointed out that the extent of bilirubinemia and accompanying icterus of new-born infants corresponds closely to the iron content of the

5. Van Creveld, S.: Icterus Neonatorum, Am. J. Dis. Child. **30**:240 (Aug.) 1925.

6. Lepehne, G.: Weitere Untersuchungen über Gallenfarbstoff in Blutserum des Menschen, Deutsches Arch. f. klin. Med. **135**:79 (Jan.) 1921.

7. Andrewes, C. H.: Clinical Study of van den Bergh's Test in Jaundice, Quart. J. Med. **18**:19 (Oct.) 1924.

8. Grulee, C. G., and Mebane, A.: The van den Bergh Test for Icterus in the Blood of Infants, Am. J. Dis. Child. **30**:219 (Aug.) 1925.

9. Yllpö, A.: Icterus neonatorum (incl. l. n. gravis) und Gallenfarbstoffsekretion beim Foetus und Neugeborenen, Ztschr. f. Kinderh. **9**:208, 1913.

10. Hess, A. F.: A Study of Icterus Neonatorum by Means of the Duodenal Catheter, Am. J. Dis. Child. **3**:305 (May) 1912.

11. Schick, B.: Der Icterus neonatorum, eine Folge des Abbaues mütterlichen Blutes, Ztschr. f. Kinderh. **27**:231, 1920.

12. Williamson, A. C.: Placental Iron and Its Relationship to Icterus Neonatorum, Surg. Gynec. & Obst. **37**:57, 1923.

placenta, with 28 mg. as the threshold above which jaundice appears, and that this element was supplied by the hemolysis of maternal and fetal blood.

Recently there has been repeated mention in the literature of the factor of blood groups in relation to various pathologic conditions, among them toxemia of pregnancy. McQuarrie,[13] following the work of Dienst,[14] observed that the major portion of the cases in his studies fell into the group in which there was interagglutination between maternal and fetal blood, especially when the serum of the mother agglutinated the red corpuscles of the infant. It was in connection with this conception that Ottenberg advanced the theory that icterus neonatorum originates similarly. More extensive case reports, such as that of Allen,[15] have disproved McQuarrie's contention. In his series, which included 479 women, Allen noted agglutination of the infant's red blood cells by maternal serum in 21 per cent of the cases, but in no instance did the fetal serum agglutinate the mother's cells.

METHOD

The developmental characteristics of the iso-agglutinins of infants were studied in a series of seventy-five cases. Blood was examined from the umbilical cord, again when the infant was from 7 to 10 days of age and finally after 6 months. The first two periods alone are pertinent here, since it is within their limits that the inception of jaundice takes place and frequently terminates. Blood from the mother was analyzed in a similar manner for factors in agglutination at the time of delivery and at the second period, complete blood groupings being carried out as well as crossagglutination tests between mother and infant. The details of the methods employed as well as the results obtained are published elsewhere.[16] With this data available, observations were simultaneously made during the first ten days as to the incidence, depth and duration of jaundice. Through the correlation of these observations, it was possible to determine whether incompatibility between the blood groups of mother and infant was of any etiologic significance in icterus neonatorum.

RESULTS

In all but three of the seventy-five cases, the patients were studied from birth without reference to the possibility of developing jaundice. The three were first seen in the nursery after the onset of jaundice and were included because their cases were so representative. Five of the babies in the series were born prematurely. Twenty-two of the seventy-two infants developed unquestionable icterus, but in one it was

13. McQuarrie, I.: Iso-agglutination in New-Born Infants and Their Mothers, Bull. Johns Hopkins Hosp. **34**:51, 1923.

14. Dienst, A.: Das Eklampsiegift, Zentralb. f. Gynäk. **29**:353 (March) 1905.

15. Allen, W. M.: Interagglutination of Maternal and Fetal Blood in the Late Toxemias of Pregnancy, Bull. Johns Hopkins Hosp. **38**:217 (March) 1926.

16. Smith, C. H.: Iso-Agglutinins in the New-Born: With Special Reference to Their Placental Transmission, Am. J. Dis. Child., this issue, p. 54.

due to a biliary anomaly as determined by later operation. The cases were noted as slight, moderate and marked, and though only five were of the first variety, they all presented unmistakable pigmentation of the skin and sclera. Except for the instance in which there was congenital malformation, all stools were a normal brown. The incidence of jaundice, the four cases being excluded, was therefore 29.5 per cent. This is less than the percentage usually stated and is probably due to the small number of premature infants in the series and the more rigid criteria for the presence of icterus.

The blood of the baby and that of the mother were regarded as incompatible only in those instances in which definite crossagglutination reactions were obtained. Caution was exercised in designating a specimen of infant's blood as belonging to group O.[17] If the cells were not agglutinated by group A and B serums, the blood did not necessarily fulfil the requirements of this group unless the serum was tested against group A and B cells to determine the presence of the α and β isoagglutinins. On the other hand, the blood of an infant that has not as

TABLE 1.—*Incidence of Icterus Neonatorum with Relation to the Compatibility of Blood Groups*

	Total	Number Icteric	Percentage	Marked Icterus
Compatible	59	17	28.8	9
Incompatible	15	8	53.3	2

yet developed sufficiently to be classified in a definite group is compatible with that of the mother, provided that during the period in which the icterus prevails, no agglutinogen or iso-agglutinin appears with which the respective blood qualities of the mother can interact. The transition from a group apparently the same as that of the mother (group O) to one in which her serum could agglutinate the cells of her infant (groups A and B) within the first ten days occurred in two of the cases, and icterus developed in both. These cases have been described more fully elsewhere.[16]

Incidence of Icterus Neonatorum with Relation to the Compatibility of Blood Groups.—It is obvious from the figures in table 1, that icterus neonatorum is twice as common in the incompatible group. In addition, the most intensely jaundiced infants were more numerous among those whose blood was entirely compatible with that of the mother. If cross-agglutination of incompatible blood constitutes the fundamental process in the causation of icterus neonatorum, a difference in blood groups

17. In this paper, as in the preceding, the letters O, A, B, AB, have been substituted for the Jansky numbers I, II, III, IV, respectively. The letters signify the agglutinogens present in the red blood cells of each group.

should be manifest in every instance, regardless of the size of the series. One cannot deny, however, that when interagglutination takes place between the blood of the mother and that of the fetus or new-born infant, it is not without effect. One must include this process with those which in causing destruction of red blood cells are also instrumental in producing jaundice. The greater frequency of icterus neonatorum in the incompatible group indicates that cross agglutination probably plays an accessory rôle in its development.

Isohemolysins and Icterus Neonatorum.—Since icterus neonatorum is so closely bound up with hemolysis, the blood isohemolysins were also investigated. Concurrent with the tests for blood groups, one is often able to observe the presence of specific isohemolysins. There is but meager evidence that the latter can occur independently of the iso-agglutinins in human blood. The hemoglobinuria and jaundice that

TABLE 2.—*Relation of Isohemolysins to Icterus Neonatorum*

		Isohemolysins				Crossagglutination of Infant's Cells by Mother's Serum	Hemolysis of Infant's Cells by Mother's Serum
		In Mother	Percentage	In Baby	Percentage		
Compatible							
Clear	42	11	....	9	....	.	.
Jaundiced	17	5	....	2	....	.	.
Total	59	16	26.6	11	18.3	.	.
Incompatible							
Clear	7	5	....	2	....	6	2
Jaundiced	8	6	....	1	....	7	4
Total	15	11	73.3	3	20.0	13	6

follow the transfusion of incompatible blood indicate that hemolysins are probably active even though preliminary tests fail to reveal them. Ottenberg and Thalhimer,[18] however, in experimental transfusion performed in the cat found a complete correspondence between test-tube and intravascular hemolysis. Quantitative differences in human as compared with animal complement may account for this discrepancy.

Table 2 shows the frequency with which isohemolysins appeared in the blood of mother and infant during the first ten days. Jones[19] obtained much higher figures, but this can probably be attributed to technical differences. According to this author, slight degrees of hemolysis may be detected by placing cells and serum in contact with each other for two hours, after which the preparation is centrifugalized.

18. Ottenberg, R., and Thalhimer, W.: Studies in Experimental Transfusions, J. M. Research **33**:213, 1915.

19. Jones, B. B.: Isohemolysins in Human Blood, with Especial Reference to the Blood of the New-Born, Am. J. Dis. Child. **22**:598 (Dec.) 1921.

Williams [20] states that he could demonstrate hemolysis whenever agglutination took place, the reason for failure to observe it in every case being due to low hemolysin titer. The activity of the latent hemolysin can be brought out by supplying sufficient complement or by increasing the amount of serum. This, however, can hardly be compared with isohemolytic reactions in which the natural quantitative relationships of hemolysin and complement are maintained.

One would expect that when the blood of the mother and infant do not match, the existence of isohemolysins against the cells of either would be conducive to the appearance of jaundice. Owing to the infrequency and low titer of isohemolysins and iso-agglutinins in the blood from the cord and from the infant 10 days old, one may discount their importance as factors in crossagglutination and hemolysis. On the other hand, there is a greater chance for the baby's cells to be agglutinated and hemolyzed because of the earlier development of their cell receptors. Also, in the serum of the mother of group O, which statistically is the most common blood group, the two iso-agglutinins and often isohemolysins are present. The latter were present most often in the blood of incompatible mothers, where one would reasonably expect that they should be operative in the production of jaundice. Despite the hemolysis of infant's cells by the serum of the mother in vitro in six cases, clinical jaundice was absent from two of these. It may be that the demonstration of hemolysins outside of the body does not always bespeak their presence in the circulation or that they may be active without causing such obvious changes as jaundice.

It is noteworthy that in five of the cases in the incompatible group in which the mother's serum contained both iso-agglutinins and hemolysins, crossagglutination of the infant's cells took place without simultaneous hemolysis. As these isohemolysins were effective against other cells of the same group, doubt is thrown on the antigenic action of the fetal cells in causing the production of hemolysin in the mother through a process of immunization.

In order that the iso-agglutinins of the mother may be effective they must enter the circulation of the fetus, and this presupposes a permeability of the placenta or an admixture of blood through a break in its structure. Hess [21] suggests that during labor a continuity between the circulations of mother and fetus may be established through placental tears. None of the placentas in the present series revealed any imper-

20. Williams, W. C.: Importance of Blood Groups in Complement Fixation Reactions, J. Exper. Med. **32**:159, 1920.

21. Hess, R.: Ueber Iso-agglutinine beim Neugeborenen, Deutsche med. Wchnschr. **47**:241, 1921.

fections on gross examination. For the passage of iso-agglutinins through an intact placenta there is evidence as presented in another study.[16]

It might, however, be supposed that in cases of pathologic labor with the possibility of trauma to the placenta a means of communication would be afforded between the two circulations. An analysis of this factor in its bearing on icterus is shown in table 3.

It is observed that in the incompatible group in which this event should play an important part, there was but one difficult labor, and the baby in this case was not jaundiced. In the compatible group there is not a sufficiently striking difference between jaundiced and non-jaundiced infants to demonstrate the influence of the type of labor. With blood groups that do not allow for crossagglutination, the connection between pathologic labor and icterus neonatorum must be explained differently. Schwartz [22] and Deluca [23] ascribe icterus to the absorption of traumatic hemorrhages encountered during labor. While this assump-

TABLE 3.—*Relation of Pathologic Labor to Icterus Neonatorum*

	Totals	Pathologic Labor	Percentage
Compatible			
Jaundiced	18	7	38.8
Clear	42	13	30.9
	60		
Incompatible			
Jaundiced	8	0	....
Clear	7	1	....
	15		

tion cannot be contradicted, it does not hold universally true. With five premature infants in this series, all abnormally delivered and with no incompatibility of blood groups, jaundice developed in only one. Again, thirteen of the forty-two in the compatible group were delivered abnormally without any signs of icterus.

In the last analysis, if incompatibility of the blood is an essential factor in the destruction of red blood cells, crossagglutination must occur in large part before or at the time of birth when the actual admixture of blood between mother and fetus is possible. It is improbable that the iso-agglutinins and isohemolysins introduced into the circulation of the fetus at this time remain in new-born infants sufficiently long to manifest their influence for the entire period during which icterus prevails. Again, it is difficult to reconcile the day or two directly after birth before icterus sets in with the simultaneous agglutination and hemolysis of infant's cells that is supposedly going on unless it is explained by

22. Schwartz, P.: Zur Frage des Icterus neonatorum, Ztschr. f. klin. Med. **100**:117, 1924.

23. Deluca, F. A.: Ueber den "symptomatischern" Icterus neonatorum, München. med. Wchnschr. **69**:1254, 1922.

Schick's [11] view that the functional immaturity of the skin at this time prevents the appearance of icterus. There is, however, the possibility that the red blood cells of the fetus and new-born may be damaged by the iso-agglutinins and hemolysins received from the admixture of incompatible blood from the mother and that their destruction proceeds slowly throughout the period of icterus.

SUMMARY

In a series of seventy-five cases in which the development of iso-agglutinins in the blood of new-born infants was studied, the incidence of icterus neonatorum was also investigated to determine whether it depends on the incompatibility of blood groups between mother and infant.

Icterus neonatorum appeared more often when the blood groups of the mother and of the new-born infant did not match, but this relationship was not always demonstrable.

Isohemolysins appeared infrequently in the serum of the new-born infant and most often in the blood of the incompatible mother. The isohemolysins of the mother were not always effective against the cells of her own infant, although they were active against others of a similar group.

Jaundice appeared in the infant in four of six cases in which the red cells were hemolyzed by the serum of the mother.

Pathologic labor which might be assumed to provide a means of securing admixture of maternal and fetal blood could not be shown to have any bearing on the occurrence of icterus neonatorum.

CONCLUSIONS

The results from the series of cases studied do not furnish proof that incompatibility of blood group between mother and child plays a primary rôle in the etiology of icterus neonatorum. Evidence has been presented, however, to show that interagglutination may serve as an accessory factor in the production of this condition.

113 East Eighty-First Street.

THE VOLUME OF THE BLOOD

I. THE USE OF THE THERMOCOUPLE FOR DETERMINING THE FREEZING POINT OF A SMALL QUANTITY OF FLUID *

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Investigation of the freezing point of the blood serum in infants has been greatly restricted owing to the necessity of using, with the ordinary Beckmann thermometer, relatively large quantities of fluid, from 10 to 20 cc. Although the Beckmann apparatus has been modified by Guye and Bogden,[1] Burian and Drucker [2] and others for use with small quantities of fluid, we have not been able to obtain consistent results with any of the modified Beckmann thermometers that we have been able to obtain. In 1911, Salge [3] used a thermocouple to determine the freezing point of blood serum of children, and recently Bishop [4] described a method involving the use of a potentiometer by which the freezing point of as little as 0.2 cc. of fluid can be determined.

The method here described is the one used by us in making determinations of the freezing point of blood serum in a series of cases reported elsewhere.[5] In principle, the method is a modification of that of Salge, but its simplicity of operation is an advantage over the latter.

APPARATUS

The apparatus consists, essentially, of a thermocouple, a sensitive galvanometer with a scale and a variable resistance and containing vessels for the freezing material and the solution, the freezing point of which is to be determined. The arrangement of the apparatus is shown in the accompanying diagram.

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* Received for publication, March 8, 1928.

* From the Pediatric Service and the Thorndike Memorial Laboratory of the Boston City Hospital, and the Pediatric Department of the Harvard Medical School.

1. Guye, P. A., and Bogden, S.: Methodes rapides pour l'analyse phsico-chimiques des liquides physiologiques, J. de chim. phys. **1**:379, 1903.

2. Burian, R., and Drucker, K.: Gefrierpunktmessungen an Kleinen Flüssigkeitsmengen, Zentralbl. f. Physiol. **23**:772, 1910.

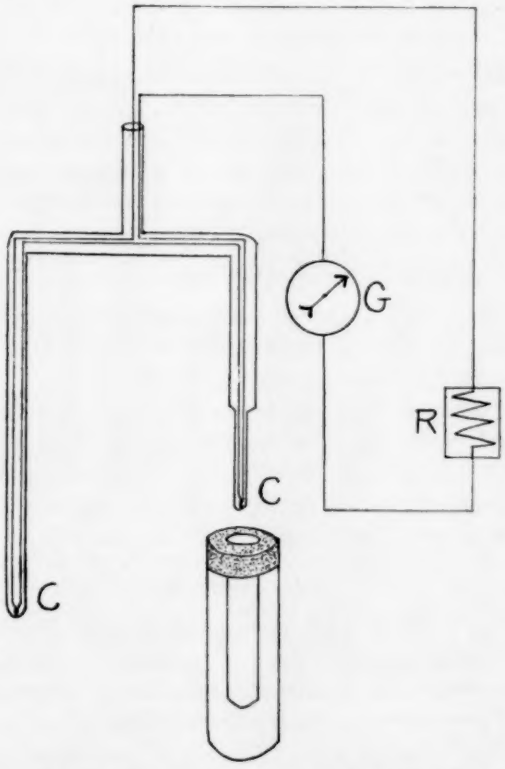
3. Salge, B.: Die physikalischen Erscheinungen des Blutes beim gesunden und kranken Saügling, Ztschr. f. Kinderh. **1**:426, 1911.

4. Bishop, George H.: Body Fluid of the Honey-Bee Larva, J. Biol. Chem. **58**:543, 1923-1924.

5. Darrow, Dan C., and Buckman, Thomas E.: Observations on the Volume of the Blood: II The Blood Volume and Concentration of Crystalloids and Electrolytes in Dehydration and Edema, Am. J. Dis. Child., to be published.

1. The thermocouple consists of five junctions of constantan and copper wire, connected in series, in the closed end of each of the L-tubes. The leads passing out through the U-tube are attached to metal plates which make connections which leads to the galvanometer and the variable resistance. Each of the five double junctions produces a difference of potential of about 40 microvolts per degree difference in temperature between the couples.

2. The galvanometer should have a sensitivity of 0.2 microvolt and a critical external damping resistance of about 40 ohms. A distance of 5 mm. on the scale should correspond to about 1 microvolt. These requirements are met by the



Scheme of arrangement of apparatus. *C* indicates the junctions of the thermocouple; *G*, galvanometer and *R*, variable resistance box.

Leeds and Northrop galvanometer, type H. S. 2285b. The galvanometer must be protected from air currents which may influence its temperature and should rest on a grounded metal support.

3. A scale 1 meter long is the most convenient form for use with the type of galvanometer here employed, but a shorter scale may be used satisfactorily if sufficient resistance is introduced into the circuit. The scale must be maintained at a fixed distance from the galvanometer.

4. A thermos bottle or Dewar flask makes a convenient receptacle for the mixture the temperature of which is to be maintained at 0 C. This mixture consists of

a mush made of shaved ice and distilled water. It is not necessary to use ice made from distilled water provided the ice is washed in distilled water.

The freezing chamber consists of a small test tube (100 mm. by 13 mm.) fitted through a cork into a larger test tube. The latter is clamped in a beaker containing the freezing mixture of ice, salt and water. Stirrers, of course, are necessary for both the freezing mixture and the mixture to be frozen. For the former a stiff wire suffices, while for the latter a platinum loop fused to a piece of glass tubing may be used.

5. The variable resistance should consist of a standard resistance box giving varying resistances of from 1 to 10,000 ohms.

PRINCIPLE OF THE METHOD

The principle underlying this method of determination of temperature is too well known to require description here. In the particular apparatus used, the sensitivity of the galvanometer was 0.2 microvolt. Since, then, each of the five double junctions of constantan and copper wire corresponds to about 40 microvolts per degree difference in temperature, it follows that the sensitivity of the apparatus is approximately

$$\frac{0.02}{5 \times 40} = 0.001^{\circ} \text{ C.}$$

Moreover, since each microvolt corresponds approximately to 5 mm. on the galvanometer scale, a temperature difference of 1 C. would be represented on the galvanometer scale by 200 by 5 mm., or 1 m. Hence, if one set of the wire couplings is maintained at 0 C. and the other set is immersed in the mixture the freezing point of which is to be determined, then the distance in millimeters traversed by the light beam from the galvanometer mirror on the scale will represent in thousandths of a degree below zero the freezing point of the unknown mixture.

PROCEDURE

The details of procedure are enumerated below. Before determinations of the freezing point are made, it is necessary to standardize the apparatus empirically by means of a Beckmann thermometer which itself has been previously carefully standardized. That is, the freezing point of a number of solutions of different concentration are determined first by means of the Beckmann apparatus. Each solution is then frozen in the freezing chamber of the apparatus already described and the deflection of the light beams on the galvanometer scale is noted. It is then possible to determine the factor by which the reading of the galvanometer scale must be multiplied in order to reckon the freezing point of any solution the freezing point of which is to be determined. In standardizing the apparatus that we constructed, solutions of barium chloride were used and their freezing points were determined by means of a Beckmann thermometer standardized by the United States Bureau of Standards. The consistency of our results is indicated by the accompanying table.

In practice, the following procedure has been found convenient for determining the freezing point of a liquid with this apparatus:

1. A mixture of crushed ice and water is placed in a thermos bottle or Dewar flask and one end of the thermocouple is immersed in this mixture the temperature of which is 0 C. About 3 ml. of the fluid, of which the freezing point is to be determined, is now placed in the small test tube which is fixed in position in the freezing chamber containing ice, water and rock salt. The other end of the thermocouple is immersed in the liquid in the test tube and the small stirring rod introduced.

2. The "zero" position of the light beam from the galvanometer is now adjusted to fall near one end of the scale and the exact position noted. A resistance of several thousand ohms is then introduced into the circuit and the connections between the thermocouple and the galvanometer are made.

3. As soon as the connections are made the light beam will be deflected in one direction, owing to the fact that the liquid in the test tube is warmer than the mixture in the thermos bottle. After a few moments, during which the liquid in the test tube and the freezing mixture are stirred constantly, the light beam will

Consistency of Results of Standardization of Apparatus

Barium Chloride Solution	Freezing Point Determined by Beckmann Apparatus C.	Reading of Galvanometer Scale (Cm.)	Factor
1	0.423	18.8	0.0224
2	0.481	21.2	0.0226
3	0.499	22.3	0.0224
4	0.583	26.1	0.0224
5	0.637	28.6	0.0223
6	0.685	30.9	0.0222
7	0.720	32.1	0.0224
8	0.774	35.2	0.0220

begin to move in the opposite direction; it passes through the zero point, thus indicating that the liquid in the test tube has become colder than zero. As soon as this occurs, all but a few hundred ohms of resistance should be thrown out of the circuit. When the liquid in the test tube starts to freeze, the light beam will begin to move back toward the zero point because some supercooling has occurred, and as soon as freezing starts the ice in the test tube becomes slightly warmer. When the light beam thus begins to move back toward the zero point, the resistance should be reduced to the amount used in standardizing the apparatus. The freezing point of the liquid in the test tube is indicated by the position nearest the "zero" point reached by the light beam after freezing of the liquid begins.

4. Varying resistances are used merely to keep the light beam on the scale. The most convenient resistances to be used will vary according to the length of the scale and the position thereon selected for the zero point when the apparatus is standardized. In practice it is easy to determine, after a few trials, the appropriate resistance for each step in the procedure.

5. It is of the utmost importance to stir the unknown liquid after freezing has begun. The freezing mixture also must be stirred from time to time.

6. We did not adopt the practice of "seeding" with ice crystals the liquid to be frozen. By this means, of course, much of the supercooling could have been avoided, but accurate duplicate determinations on the same specimen could

not have been made, because as soon as melting occurred the added ice crystals would have diluted the solution. The error from this source probably would have been greater than the error caused by supercooling.

During the course of two years, we have made several hundred determinations of freezing points with the apparatus and technic described. Judging from our own experience, we believe that after a little practice it is possible to determine the freezing point of a liquid, using not more than 3 ml. with an error not exceeding 0.004 C. The determination may be made in less than ten minutes.

SUMMARY

A rapid, electrometric method for determining the freezing point of small quantities of fluid is described.

THE INFLUENCE OF SLEEP ON BASAL METABOLISM OF CHILDREN *

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In a previous publication,[1] we reported that the average basal metabolism determined on a group of vigorous normal children showed an increase of 10 per cent above the standards reported by Benedict.[1a] In this earlier series of experiments, the children were kept awake but strictly quiet, the kymographic record showing absence of all muscular activity. Benedict does not give figures to show the prevalence of wakefulness in the children in his series but intimates, at least, that many of them were asleep. In order to determine the degree of difference between basal metabolism while children were asleep and awake, the present investigation was undertaken.

Little work has been reported on the actual differences in the same person under these circumstances. In his study of a fasting man, Benedict [2] found an average increase of 12 per cent in the oxygen consumption while he was awake, as compared with that measured while he was asleep. In another article by the same author,[3] a difference of 6.1 and 14.8 per cent, respectively, was shown in the heat production of two infants while they were asleep and awake.

In a study of the basal metabolism of seven children, Wilson and his associates [4] reported data taken on three of them while asleep and

* Received for publication, Jan. 17, 1928.

* From the Nelson Morris Institute for Medical Research and the Sarah Morris Hospital for Children of the Michael Reese Hospital. Aided by a fund contributed jointly by the Elizabeth McCormick Fund, Mrs. Francis Neilson, Mrs. Gusta Morris Rothschild and Mr. Melville M. Rothschild.

1. Wang, C. C.; Kern, R.; Frank, M., and Hays, B. B.: Metabolism of Undernourished Children: II. Basal Metabolism, Am. J. Dis. Child. **32**:350 (Sept.) 1926.

1a. Metabolism and Growth from Birth to Puberty, Publication 302, Carneg. Inst., Washington, 1921.

2. Benedict, F. G.: A Study of Prolonged Fasting, Publication 203, Carneg. Inst., Washington, 1915.

3. Benedict, F. G.: Metabolism During Starvation and Undernutrition, New York M. J. **115**:249 (March) 1922.

4. Wilson, J. R.; Levine, S. Z., and Rivkin, H.: The Respiratory Metabolism in Infancy and in Childhood: I. Ketosis and the Respiratory Exchange in Children, Am. J. Dis. Child. **31**:335 (March) 1926.

while lying quietly awake. The heat production was found to be from 11.3 to 26.9 per cent higher while they were awake.

In estimating the basal metabolism of adult subjects on the basis of percentage of the Harris-Benedict standard, Pickworth [5] found that subjects who were sleeping soundly had an average caloric output of 70 per cent of this standard, in contrast to the second group, who showed an average of 83.9 per cent while lying quiet, with voluntary relaxation of mind and body. A third group, lying quiet and smoking, but not making a special effort at relaxation, showed an average output of 92.8 per cent. An 18 per cent increase of heat production while he was awake is reported for one person on whom figures are given for both the periods when he was asleep and awake.

Fig. 1.—Representative kymograph tracing of child

EXPERIMENTAL

Five boys and seven girls were used in this series of experiments. Their ages ranged from 4 to 10 years, and their weights, from + 5.7 to — 22.7 per cent, compared with the Baldwin-Wood height-weight-age standard. With the exception of two, all the children were below the standard for their height and age, six of them being more than 10 per cent below.

As in previous investigations,[1] Benedict's cot chamber with universal respiration apparatus was employed, the same precautions being observed. All but four of the observations were taken between 3 and 4 a. m. Some of the children slept all night in the chamber. Others, at their own request, were brought to the chamber while asleep. Means were not provided for recording the depth of sleep. How-

5. Pickworth, F. A.: Basal Metabolism as Determined by the Respiratory Exchange, Proc. Roy. Soc. London **101**:163 (March) 1927.

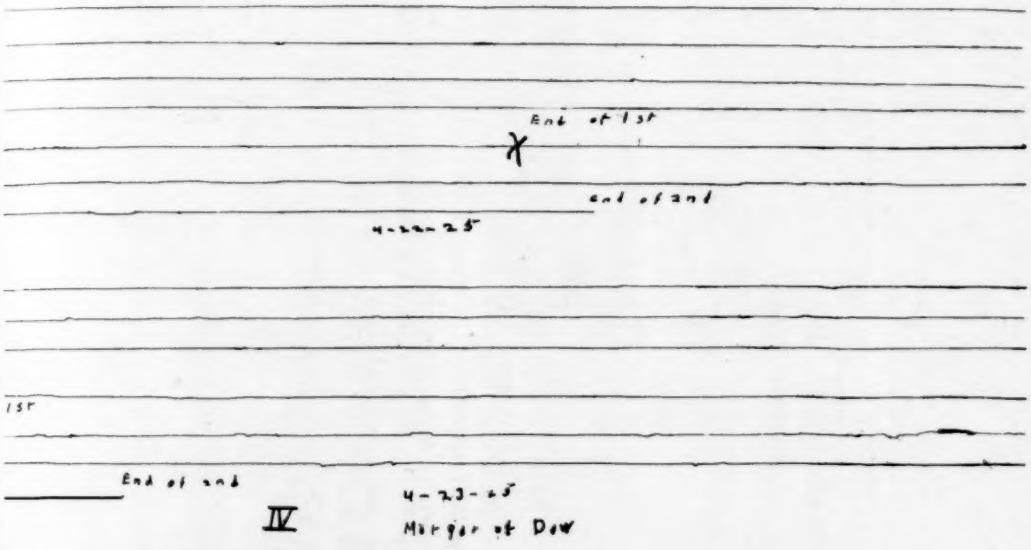
ever, the children were all motionless, and if one of them awakened during an experiment these results were discarded.

The metabolism while awake was taken either later in the morning or on another day. The kymographic records, two of which are reproduced in figure 1, show that the children were absolutely quiet during these tests.

Computations are based on the average of two duplicate determinations made during sleep, and on the two lowest of several determinations made while awake.

COMMENT

Table 1 shows that in every case a decrease in heat production took place during sleep. The percentage of difference ranged between 5.7 and 30.6, with an average of 15. Nine of the twelve children showed a decrease of more than 10 per cent. Neither age, sex nor extent of



while awake, to show absence of muscular activity.

undernutrition seemed to affect the degree of variation. The variation might have been caused by differences in the soundness of sleep, but, as previously stated, there was no means of estimating this. With the exception of one child, the pulse rate was found to decrease during sleep, the maximum decrease being 11.9 per cent. However, a correlation was not found between the decrease in the pulse rate and the decrease in the heat production, which is contrary to Benedict's [2] observations on a man during a fast lasting for thirty-one days.

Differences were not observed in the respiratory quotient, which shows that the children were in an absolute postabsorptive condition.

Table 2 shows a comparison of our results with Benedict's standards in reference to age, weight and height. As previously reported,[1] with

TABLE 1.—*Influence of Sleep on Basal Heat Production, Pulse Rate and Respiratory Quotient in Children*

Subject	Age Years	Sex*	Height (Cm.)	Weight		Heat Production Per 24 Hours				Respiratory Quotient		Pulse Rate	
				Kilograms	Deviation from Standard (Per Cent)	Awake (Calories)	Asleep (Calories)	Difference (Calories)	Difference Per Cent	Awake	Asleep	Awake	Asleep
E. S.	4	♀	101	14.0	—10.3	910	737	173	23.5	0.82	0.82	92	84
H. M.	4	♂	103	12.6	—22.7	851	770	81	10.5	0.77	0.77	70	64
B. B.	5	♀	92	11.6	—14.7	859	658	201	30.6	0.83	0.83	94	84
H. D.	5	♂	93	13.5	— 2.9	802	746	56	7.5	0.87	0.87	100	98
D. M.	5	♂	104	14.5	—13.6	868	818	50	6.1	0.79	0.79	84	78
A. G.	5	♀	108	18.1	+ 1.7	987	871	116	13.3	0.82	0.82	84	78
E. F.	6	♀	108	15.3	—14.0	868	763	105	13.8	0.83	0.83	84	80
E. F.	6	♀	111	18.0	— 2.2	927	853	74	8.7	0.83	0.83	86	82
L. M.	7	♂	117	22.1	+ 5.7	1091	968	123	12.7	0.82	0.82	86	76
M. D.	7	♀	120	19.1	—13.6	960	899	51	5.7	0.83	0.83	98	92
H. S.	9	♀	132	27.2	— 3.5	996	815	181	22.2	0.81	0.81	84	80
S. K.	10	♂	137	27.6	— 9.5	1055	839	216	25.8	0.79	0.79	78	78
Average	..	..	...	....	.....	....	...	119	15.0	0.818	0.818	87	81

* In this table and table 2 ♂ indicates male and ♀ female.

TABLE 2.—*Influence of Sleep on Basal Metabolism with Reference to Standards of Age, Weight and Height*

Subject	Age	Sex	Height (Cm.)	Weight		Deviation from Standards					
				Kilograms	from Standard Deviation (Per Cent)	Referred to Age		Referred to Weight		Referred to Height	
						Awake (Per Cent)	Asleep (Per Cent)	Awake (Per Cent)	Asleep (Per Cent)	Awake (Per Cent)	Asleep (Per Cent)
E. S.	4	♀	101	14.0	—10.3	+30.0	+ 7.6	+36.8	+10.8	+32.8	+ 5.2
H. M.	4	♂	103	12.6	—22.7	+17.4	+ 6.2	+29.5	+17.2	+ 7.1	— 3.1
B. B.	5	♀	92	11.6	—14.7	+15.3	— 1.2	+44.4	+10.6	+37.8	+ 5.6
H. D.	5	♂	93	13.5	— 2.9	+ 3.5	+ 0.4	+17.9	+10.0	+ 9.9	+ 2.2
D. M.	5	♂	104	14.5	—13.6	+12.0	+ 5.5	+22.3	+15.2	+ 8.5	+ 2.2
A. G.	5	♀	108	18.1	+ 1.7	+31.6	+16.9	+29.9	+14.1	+31.8	+16.3
E. F.	6	♀	108	15.3	—14.0	+ 9.9	— 3.4	+27.6	+12.2	+15.9	+ 1.9
E. F.	6	♀	111	18.0	— 2.2	+17.3	+ 8.0	+24.1	+14.2	+19.2	+ 9.6
L. M.	7	♂	117	22.1	+ 5.7	+30.7	+ 8.2	+19.9	+15.9	+21.8	+ 6.0
M. D.	7	♀	120	19.1	—13.6	+13.1	+ 7.7	+21.8	+15.3	+ 9.7	+ 3.8
H. S.	9	♀	132	27.2	— 3.5	+ 7.7	—10.9	+ 2.2	—16.4	+ 1.1	—17.3
S. K.	10	♂	137	27.6	— 9.5	— 1.9	—21.6	— 0.5	—20.7	— 6.6	—25.8
Average	..	..	...	....	.....	+15.6	+ 2.0	+23.0	+ 8.2	+15.8	+ 0.6

the exception of subject S. K., the results obtained with children while they were awake were all above these standards. In comparison with the standard in reference to age, eight of the twelve children used in our series of experiments are more than 10 per cent above the standard, with a maximum of 31.6 per cent and an average of 15.6 per cent; ten are more than 10 per cent above the standard for weight, the maximum

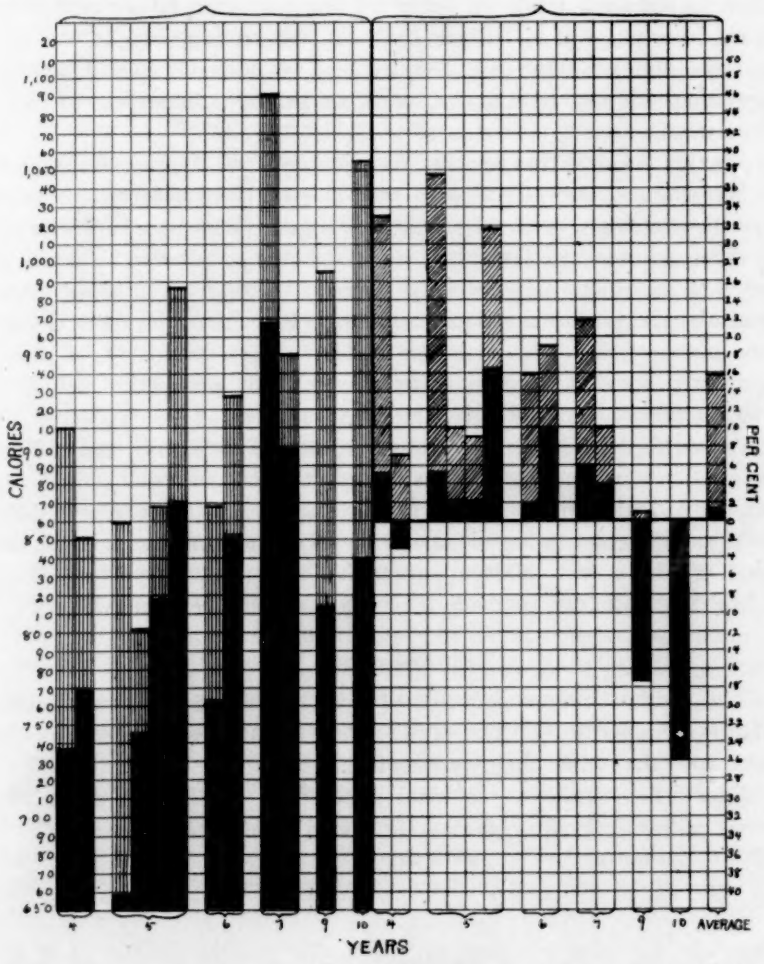


Fig. 2.—Effect of sleep on basal metabolism in children. The left half shows the calories per twenty-four hours; the right half, percentage of deviation from Benedict's standard in reference to height; the black areas indicate that the child was asleep, and the shaded areas, that the child was awake.

being 44.4 and the average, 23.0, and six are more than 10 per cent above the standard for height, with a maximum of 37.8 per cent and an average of 15.8 per cent.

The values observed during sleep agree with Benedict's standards much more closely. In reference to age, two children are more than 10 per cent below the standard, while only one is 10 per cent above. All the rest of our results fall within ± 10 per cent, with an average of + 2 per cent.

In reference to weight, two children are more than 10 per cent below the standard, while the other ten are more than 10 per cent above, giving an average of + 8.2 per cent. In reference to height, we again have two children more than 10 per cent below the standard, and one more than 10 per cent above, with an average difference of + 0.6 per cent.

Figure 2 shows that for the younger children, the results obtained during sleep agree more closely with the standard referred to height than those obtained while the child was awake; the opposite is true for the older children, aged 9 and 10 years. This may possibly be due to the fact that Benedict's standards for younger children were based largely on results obtained during sleep, while his observations on older children were more often made while the children were awake. Our results apparently show a marked difference in heat production while the children were asleep and while they were awake.

Although the number of children in our series in each age group is too small to enable us to draw any definite conclusions, it would seem that more work should be done on the standards for younger children. Since experiments during sleep can be performed only with great difficulty, standards for children comparable with those for adults should be based on observations made while the children are kept awake.

SUMMARY

The results obtained from observation of twelve children showed a definite reduction in the heat production while they were asleep as compared with that while they were awake.

Benedict's standards for basal metabolism of children agree more closely with the results obtained for young children during sleep.

ASTHMA IN CHILDREN

IV. HYPERSENSITIVENESS AND THE FAMILY HISTORY *

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With the introduction of a practical method of determining by test the reactivity of the skin to various protein substances, the influence of heredity on asthma has become a subject of special interest particularly directed to the question whether or not allergy can be acquired. The result has been to lead many workers to participate in a controversial discussion. On the one side there are those investigators who consider experimental anaphylaxis and allergy (atopy) basically identical conditions, and on the other, workers who, while agreeing that anaphylaxis is an experimental state which can be induced in animals, are dogmatically opposed to any theory which assumes that allergy can likewise be induced in the human being. In other words, they maintain that allergy can never be acquired in man and rigidly restrict the use of the term "anaphylaxis" to that experimental state induced in animals. The proponents of the latter theory agree that asthma per se is not inherited but contend that the "soil," "physiochemic make-up" or tendency to develop allergic disease is inherited. In order to avoid confusion, the terms "allergy (atopy)" and "anaphylaxis" used in this paper will be restricted to hypersensitiveness in man and in animals, respectively.

The fact that a large percentage of patients with asthma in this study show a positive antecedent family history of allergy cannot satisfactorily explain the larger incidence of negative histories even on the basis of faulty history due to ignorance of the patients, concealment or lack of knowledge of an existence of allergic disease among the antecedents, or a potentially hypersensitive antecedent whose sensitiveness was not made clinically manifest because of lack of contact with the specific sensitizing substance. A review of the literature setting forth important experimental data is therefore necessary for a better understanding of the nature of clinical hypersensitiveness and its relation to the family history.

It is to Richet (1902) that credit is due, not only for the term "anaphylaxis," but for the creation of the subject itself. The idea that anaphylaxis was the result of an antigen-antibody reaction originated in the theories of Pirquet and Schick (1903), who offered it as an explanation of the mechanism of serum sickness, the one condition which served to bridge the gap between animal and human hypersensitiveness

* Received for publication, Feb. 20, 1928.

* From the Children's Asthma Clinic, Mt. Sinai Hospital.

and which they were the first to describe fully. In 1917, Cooke, Flood and Coca [1] reported that they were unable to demonstrate any antigenic properties in timothy and ragweed pollens. These observations were viewed by these authors as a severe setback to the proposition that the mechanism of hay-fever could be explained as an anaphylactic phenomenon. Parker,[2] Alexander,[3] Walzer and Grove [4] and others showed later that guinea-pigs can be made hypersensitive to pollen, but because of the failure of all workers to demonstrate precipitins, Coca [5] held that the specific hypersensitive condition in these guinea-pigs may not be a true anaphylactic sensitization. However, Parker [6] subsequently successfully demonstrated that ragweed pollen injected into properly prepared guinea-pigs was definitely an anaphylactic antigen.

Grove and Coca [7] maintained that the active principle in pollen to which patients with hay-fever were sensitive was not a protein. Meantime, Walzer and Grove,[8] having failed to demonstrate the presence of precipitins in the serums of pollen sensitized animals, found that digestion with trypsin and dialysis did not remove the antigenic principle of ragweed pollen. However, Caulfield and his associates [9] and Bernton et al.[10] isolated (after the method of Heyl) several fractions from pollen, the active principles of which were definitely proved to be protein. The protein fractions were present in small amounts. Patients

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1. Cooke, R. A.; Flood, E. P., and Coca, A. F.: Hay-Fever. Nature of Process and of Mechanism of Alleviating Effect of Specific Treatment, J. Immunol. **2**:217 (Feb.) 1917.

2. Parker, J. T.: The Antigenic Properties of Ragweed Pollen, Proc. Soc. Exper. Biol. & Med. **18**:237 (April) 1921.

3. Alexander, M. E.: Anaphylactogenic Properties of Rye Pollen (Secale Cereale), J. Immunol. **8**:457 (Nov.) 1923.

4 Walzer, M., and Grove, E. F.: A Study of the Anaphylactogenic Properties of Aqueous Extracts of Pollens and Le Page's Glue, Proc. Soc. Exper. Biol. & Med. **21**:47 (Nov.) 1923.

5. Coca, A. F., in Tice: Practice of Medicine, Hagerstown, Md. W. F. Prior Co., 1920, vol. 6, p. 179.

6. Parker, J. T.: Production of Precipitins for Ragweed Pollen, J. Immunol. **9**:515 (Nov.) 1924.

7. Grove, E. F., and Coca, A. F.: Studies in Hypersensitiveness: XV. On the Nature of Atopens of Pollens, House Dust, Horse Dander and Green Pea, J. Immunol. **10**:471 (March) 1925.

8. Walzer, M., and Grove, E. F.: Studies in Specific Hypersensitiveness: XVI. On Antigens. A Comparative Study of the Antigenic Properties of Pollen, Eggwhite and Glue, in Guinea-Pigs, as Determined by the Intravenous and Dale Methods of Testing in Anaphylaxis, J. Immunol. **10**:483 (March) 1925.

9. Caulfield, A. H. W.; Cohen, C., and Eadie, G. S.: The Antigenic Properties of Pollen Fractions, J. Immunol. **12**:153 (Aug.) 1926.

10. Bernton, H. S.; Jones, D. B., and Osonka, F. A.: Pollen Proteins and Their Clinical Significance in Hay-Fever; Preliminary Communication, South. M. J. **20**:257 (April) 1927.

were successfully relieved of hay-fever after a course of injections with a solution of the protein fraction showing the largest positive reaction by skin test. Moreover, it was shown by Caulfield that it was possible to sensitize guinea-pigs actively and passively with great ease and regularity to the albumin-proteose and proteose fractions of pollen.

The foregoing statements give the impression that only a protein substance can be an anaphylactic antigen. However, Zinsser [11] asked, "have we not been too narrow in our definition of antigen?" It has been shown that symptoms of hypersensitiveness caused by "non-antigen" (nonprotein) materials, such as synthetic drugs, are in reality allergic and that a specific cellular reaction exists. Landsteiner's [12] supposition, that partial antigens or "haptenes" may still react specifically with antibodies without themselves having the capacity of inducing antibody formation, was wisely predicted; it was demonstrated to be a fact by the studies of Zinsser and his co-workers [13] with the so-called bacterial residue-antigen; by Avery and Heildelberger,[14] with the simple carbohydrate fractions of the total bacterial antigen, and particularly by the subsequent investigation of the Forssman antigen by Doerr and Hallauer [15] and others who have indicated that many pure lipoids may be converted into truly antigenic material by simple contact with protein.

Lewis and Loomis [16] found an increased antigenic response in guinea-pigs specifically sensitized during tuberculous infection. These observations were confirmed by Dienes and Schoenheit,[17] who also added

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11. Zinsser, H.: Hypersensitiveness, Boston M. & S. J. **196**:387 (March 10) 1927.

12. Landsteiner, K., and Simms, S.: Production of Heterogenetic Antibodies with Mixture of Binding Part of Antigen and Protein, J. Exper. Med. **38**:127 (Aug.) 1923.

13. Zinsser, H.: Tuberculin Reaction and Specific Hypersensitiveness in Bacterial Infection, J. Exper. Med. **34**:495 (Nov.) 1921. Zinsser, H., and Mueller, J. H.: Nature of Bacterial Allergies, ibid. **41**:159 (Jan.) 1925. Mueller, J. H., and Tomcsik, J.: Chemical Nature of Residue Antigen Prepared from Yeast, ibid. **40**:343 (Sept.) 1924. Mueller, J. H.: Chemical Study of Specific Elements of Tuberculin, ibid. **43**:1 (Jan.) 1926; Chemical Study of Specific Elements of Tuberculin: Preparation of Residue Antigen from Old Tuberculin, ibid. **43**:9 (Jan.) 1926.

14. Avery, O. T., and Heildelberger, M.: Immunological Relationship of Cell Constituents of Pneumococcus, J. Exper. Med. **42**:367 (Sept.) 1925.

15. Doerr, R., and Hallauer, C.: Critical and Experimental Investigations on Antigenic Function of Lipoids of Cells, Schweiz. med. Wchnschr. **55**:962 (Oct. 15) 1925; Antigenic Function of Forssman's Lipoid and other Lipoid Hepatins, Ztschr. f. Immunitätsforsch. u. exper. Therap. **47**:291, 1926.

16. Lewis, P. A., and Loomis, D.: Allergic Irritability: Formation of Antisheep Hemolytic Amboceptor in Normal and Tuberculous Guinea-Pig, J. Exper. Med. **40**:503 (Oct.) 1924.

17. Dienes, L., and Schoenheit, E. W.: Local Hypersensitiveness: I. Sensitization of Tuberculous Guinea-Pigs with Eggwhite and Timothy Pollen, J. Immunol. **24**:9 (July) 1927.

that skin sensitiveness was increased during tuberculous infection as well as during vaccination against smallpox.[18] Passive transfer of local hypersensitiveness to tuberculous and nontuberculous animals with the blood serums of specifically sensitized tuberculous guinea-pigs was demonstrated.[19] In summary, Dienes[20] remarked that if a similar increase of the response can be observed in the course of other infectious diseases, then the importance of it for the development of immunity and the symptoms of diseases is evident. In this connection, from the clinical standpoint, I[21] reported that pertussis, acute pneumonia, measles and scarlet fever, collectively, were responsible for initiating the onset of asthma in 35 per cent of a series of 100 children.

Ratner, Jackson and Gruehl[22] successfully demonstrated induced anaphylaxis in the guinea-pig under conditions that were regarded as normal, i.e., without the introduction of a substance by direct injection. The experimental data in the animal and clinical evidences in the human being were shown to be so closely related as to suggest the point of view that anaphylaxis in the animal and asthma in the human subject are fundamentally the same. The evidence presented supports the theory of "acquired sensitization in the human being."

Praussnitz and Küster[23] demonstrated that specific sensitiveness could be passively transferred locally by the intracutaneous injection of blood serum of a person sensitive to protein to the skin of a person not sensitive to the protein. In order to avoid the term "antibody" for the sensitizing property contained in the blood serum, Coca and Grove[24] suggested the noncommittal term "atopic reagin."

Coca and Grove[24] were not able to demonstrate atopic reagins in the serums of persons sensitive to drugs (chemically known substances).

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18. Dienes, L., and Schoenheit, E. W.: Local Hypersensitiveness: III. Hypersensitiveness of Guinea-Pigs Treated with Eggwhite During Smallpox Vaccination, J. Immunol. **24**:53 (July) 1927.

19. Dienes, L., and Schoenheit, E. W.: Local Hypersensitiveness: II. The Transfer of Local Hypersensitiveness of Tuberculous Guinea-Pigs with the Blood Serum, J. Immunol. **24**:43 (July) 1927.

20. Dienes, L.: Local Hypersensitiveness: IV. General Consideration, J. Immunol. **24**:61 (July) 1927.

21. Peshkin, M. M.: Asthma in Children: III. The Incidence and Significance of Various Diseases and Infections, and of Tonsillectomy and Adenoidectomy, Am. J. Dis. Child. **33**:880 (June) 1927.

22. Ratner, B., Jackson, H. C., and Gruehl, H. L.: Respiratory Anaphylaxis. Sensitization, Shock, Bronchial Asthma and Death Induced in the Guinea-Pig by the Nasal Inhalation of Dry Horse Dander, Am. J. Dis. Child. **34**:23 (July) 1927.

23. Praussnitz, C., and Küster, H.: Centralbl. f. Bakteriol. Orig. **186**:160, 1921.

24. Coca, A. F., and Grove, E. F.: Studies in Hypersensitiveness: XIII. A Study of Atopic Reagins, J. Immunol. **10**:445 (March) 1925.

Biberstein,[25] however, succeeded with arsphenamine, bismuth, a brand of amidopyrene U. S. P., garlic, iodine, potassium iodide, acetyl-salicylic acid and acetophenetidin.

Coca [26] favored the point of view that the demonstration of reagins in the blood of hypersensitive persons was strictly subject to atopic inheritance. A positive skin reaction to a protein obtained in a person whose serum fails to demonstrate the presence of atopic reagin was regarded as a nonspecific or pseudoreaction. These views, however, have been abandoned since Rackermann and Stevens [27] demonstrated that the serum of worm infested subjects was capable of passively sensitizing normal skin to worm extract Fineman and I [28] found that atopic reagin could not be demonstrated in the serum of patients with negative skin reactions but with positive pollen histories. Positive reactions were obtained in all by ophthalmic test. (Dry pollen for the scratch method and pollen extract up to a concentration of 0.25 mg. of nitrogen per cubic centimeter for the intradermal method were used. The technic of the ophthalmic test with dry pollen has been described in a previous study.[29])

As a result of the foregoing experimental evidence, the criteria advanced by Coca in support of his views on this subject have been nullified to the extent that Coca [30] himself concluded that "the atopic group is thus left with only one clear bond of union, namely, the bond of heredity."

The material for this study is based on 285 consecutive cases of asthma, 89 per cent of which were in Jewish children (boys, 65 per cent; girls, 35 per cent) ranging in age from 3 months to 14 years. Two families accounted for two children each and one for three children. In order to avoid duplicating the family history, these seven cases were excluded from the statistical data, thus leaving 278 cases of asthma to form the basis of this study.

The importance of obtaining a reliable family history of allergy (asthma, hay-fever, eczema, angioneurotic edema and urticaria) from

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25. Biberstein, H.: Passive Transfer of Hypersensitiveness to Chemcially Known Substances, Ztschr. f. Immunitätsforsch. u. exper. Therap. **48**:297, 1926.

26. Coca, A. F.: Relation of Atopic Hypersensitiveness (Hay-Fever, Asthma) to Anaphylaxis. Review of Recent Literature, Arch. Path. **1**:96 (Jan.) 1926.

27. Rackermann, F. M., and Stevens, A. H.: Skin Tests to Extracts of Echinococcus and Ascaris, J. Immunol. **13**:389 (June) 1927.

28. Peshkin, M. M., and Fineman, A. H.: Asthma in Children: VIII. A Comparative Study of the Direct and Indirect Methods of Skin Testing with the Scratch and Intradermal Tests, to be published.

29. Peshkin, M. M.: Asthma in Children: I. Etiology, Am. J. Dis. Child. **31**:763 (June) 1926.

30. Coca, A. F.: Studies in Hypersensitiveness: XXIX. On the Influence of Heredity in Atopy, J. Lab. & Clin. Med. **12**:1135 (Sept.) 1927.

the parents of these children was recognized. A system of education was instituted whereby the parents were made familiar not only with the various clinical phases of allergic disease but with the scope and purpose of the treatment selected for their child. After the patients had been under observation for from one to two years, it was felt that a questionnaire covering the family history submitted to the parents would be intelligently and unhesitatingly answered. This surmise was evidently correct, since 18 per cent of the family histories that were recorded as negative when the patients first came under observation were now changed to positive. Antecedents with a history of onset of asthma after the age of 50 were regarded as positive. It is reasonable to assume, then, that the incidence of positive and negative antecedent family histories of allergy recorded in this series is representative of this class of patients.

In children with various allergic diseases, Schloss,[31] Taylor,[32] Rowe,[33] Balyeat [34] and others reported the incidence of positive family histories as ranging from 59 to 70 per cent.

In patients of all ages with asthma associated with or without hay-fever, the family history was found positive in 27 per cent of the cases reported by Piness,[35] in 48 per cent by Adkinson,[36] in 58 per cent by Cooke and Vander Veer [37] and Rackemann [38] and in 59 per cent by Spain and Cooke.[39]

Depending on the age, age of onset, environment, nationality, and even the type of allergic disease, the positive antecedent histories reported by other authors ranged down to as low as 10 per cent.

In this series of 278 children each of whom was tested by the scratch method with at least sixty-five proteins, 189 were found protein sensitive

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31. Schloss, O. M.: Allergy in Infants and Children, Am. J. Dis. Child. **19**:433 (June) 1920.

32. Taylor, W. M.: Bronchial Asthma in Children, South. M. J. **19**:330 (May) 1926.

33. Rowe, A. H.: Bronchial Asthma in Children and Young Adults, Am. J. Dis. Child. **31**:51 (Jan.) 1926.

34. Balyeat, R. M.: Hay-Fever and Asthma, Philadelphia, F. A. Davis & Co., 1926.

35. Piness, G.: Etiology and Treatment of Bronchial Asthma, Northwest Med. **22**:1 (Jan.) 1923.

36. Adkinson, J.: The Behavior of Bronchial Asthma as an Inherited Character, Genetics **5**:363, 1920.

37. Cooke, R. A., and Vander Veer, A., Jr.: Human Sensitization, J. Immunol. **1**:201 (June) 1916.

38. Rackemann, F. M.: Clinical Study of One Hundred and Fifty Cases of Bronchial Asthma, Arch. Int. Med. **22**:517 (Oct.) 1918.

39. Spain, W. C., and Cooke, R. A.: Studies in Specific Hypersensitiveness: XI. The Familial Occurrence of Hay-Fever and Bronchial Asthma, J. Immunol. **9**:521 (Nov.) 1924.

and the remainder nonprotein sensitive. The antecedent family history to allergy was positive in 40 per cent of the protein sensitive and in 45 per cent of the nonprotein sensitive group, a total incidence of 42.5 per cent.

SUMMARY OF THE CASES

The accompanying table is a summary of the antecedent family history of all the patients in this series in relation to the age at which the onset of asthma occurred.

Chart 1 shows the number of patients of the protein sensitive and nonprotein sensitive groups in relation to the age of onset of asthma. It shows that the onset of asthma is more frequent at 1 year than at any other age; that as the children approach the age of 13 the allergic

The Antecedent Family History in Protein Sensitive and Nonprotein Sensitive Children with Asthma in Relation to the Age of Onset

	1*	2	3	4	5	6	7	8	9	10	11	12	13	14	Total
Protein Sensitive Group															
Age at Onset of Asthma.															
Positive History.....	22	16	10	9	8	3	1	2	5	1	0	0	0	0	77
Negative History.....	22	26	12	11	11	9	6	4	7	2	1	0	1	0	112
Total	44	42	22	20	19	12	7	6	12	3	1	0	1	0	189
Nonprotein Sensitive Group															
Positive History	13	5	7	1	2	4	3	3	1	0	0	0	1	0	40
Negative History.....	18	6	7	4	1	1	4	3	1	2	0	1	1	0	49
Total	31	11	14	5	3	5	7	6	2	2	0	1	2	0	89
Protein Sensitive and Nonprotein Sensitive Groups															
Total Positive Histories..	†35	21	17	10	10	7	4	5	6	1	0	0	1	0	117
Total Negative Histories.	40	32	19	15	12	10	10	7	8	4	1	1	2	0	161
Total Positive and Negative Histories.....	75	53	36	25	22	17	14	12	14	5	1	1	3	0	278

* Includes all cases from 3 months to 1 year.

† A positive bilateral family history of allergy was obtained in only eight instances, as follows: protein sensitive group, two at 1 year, one each at 2, 3, 6 and 7 years; nonprotein sensitive group, one each at 2 and 13 years.

and nonallergic incidences which run parallel seem to become progressively less; that during the first five years of life the onset of asthma occurs in 78 per cent of the protein sensitive and in 72 per cent of the nonprotein sensitive groups; that in the second five years the age of onset of asthma occurs in 21 and 24 per cent of the allergic and nonallergic groups, respectively; after 10 years of age the onset of asthma in either group is not more than 2 per cent.

Chart 2 shows the incidence of positive and negative antecedent family histories in the patients of the protein sensitive group in relation to the age of onset of asthma. It shows that the incidence of positive family histories is larger with the onset of asthma at 1 year than at any other age, which also applies to the incidence of negative family histories; that during the first five years of life 34 per cent of the cases (unilateral, 32; bilateral, 2) exhibit a positive family history: that during the second five years of life only 7 per cent (unilateral, 5; bilateral, 2)

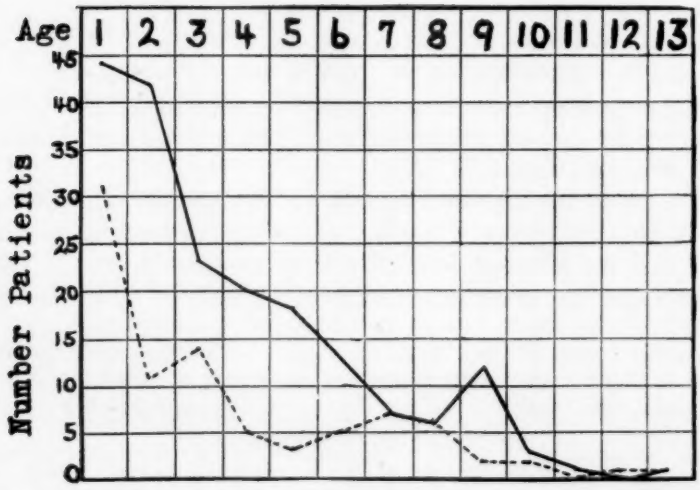

Chart 1.—The number of patients of the protein sensitive group (plain line) and of the nonprotein sensitive group (broken line) in relation to the age of onset of asthma.

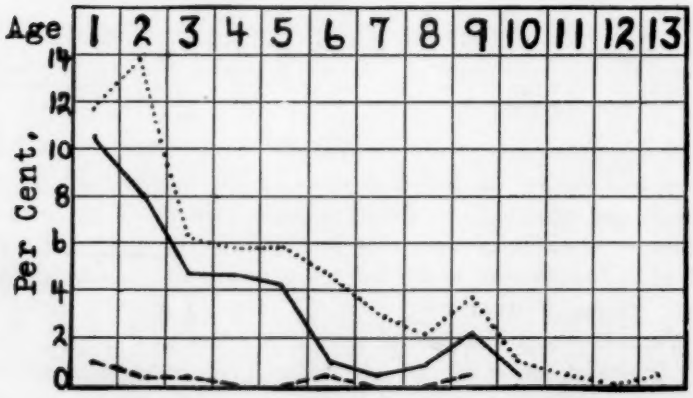

Chart 2.—The incidence of positive and negative antecedent family histories in children of the protein sensitive group in relation to the age of onset of asthma. In this chart and in charts 3, 4 and 5, the solid line indicates positive unilateral; the dash line, positive bilateral and the dotted line, negative.

are positive; and, after ten years, none. The incidence of negative family histories during the first five years of life is 44 per cent, in the second five years 15 per cent and after ten years only 1 per cent.

In the series reported by Spain and Cooke [39] are fifty-six cases comparable to those recorded in this study, which are shown in chart 3. It shows the incidence of positive family histories with the onset of allergic asthma (with or without hay-fever) during the first five years of life to be 54 per cent (unilateral 34, bilateral 20); in the second five years, 21 per cent (unilateral 17.8, bilateral 3.5) and after ten years, only 1.7 per cent (unilateral), the total incidence being 77 per cent (unilateral 53, bilateral 24). It is of interest to note that the total incidence of negative family histories of 23 per cent is entirely accounted for during the first five years of life.

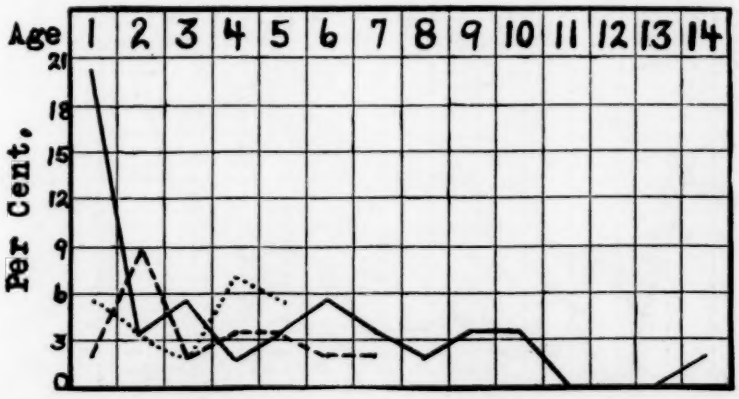

Chart 3.—The incidence of positive and negative antecedent family histories in children seen prior to 15 years of age with allergic asthma in relation to the age of onset from the series reported by Spain and Cooke.[39]

Of further interest in the report by Spain and Cooke [39] are forty adults in whom the onset of asthma dated back from childhood. The average age of these patients was 29.17 years and the average number of years that had elapsed between the onset of asthma and the age when first seen was 22.4. With the onset of asthma during the first five years of life, the family history was positive in 22.5 per cent (unilateral 20, bilateral 2.5); during the second five years, in 17.5 per cent (unilateral 12.5, bilateral 5), and after ten years, the family history was positive in 15 per cent (all unilateral), a total incidence of 55 per cent (unilateral 47.5, and bilateral 7.5). The negative family history with the onset of asthma during the first and second five year periods of life was 17.5 per cent for each period, and after ten years it was 10 per cent, a total incidence of 45 per cent. If the curves representing the incidence of positive and negative family histories in relation to the age of onset of

asthma were drawn, they would be irregular and would not resemble in any way the contour of those seen in charts 2 and 3, a fact that is of some significance.

Chart 4 shows the incidence of positive and negative antecedent family histories in patients of the nonprotein sensitive group in relation to the age of onset of asthma. The largest incidence of positive and negative family histories occurred with the age of onset at 1 year, representing 14.6 and 20.2 per cent, respectively. With the onset of asthma during the first five years of life, a positive history was obtained in 31.1 per cent (unilateral 30, bilateral 1.1) and negative in 40 per cent. With the age of onset at from 5 to 10 years, a positive history was obtained in 13.1 per cent (unilateral 12, bilateral 1.1) and negative in 12 per cent. After ten years, the family history was negative in 2.2

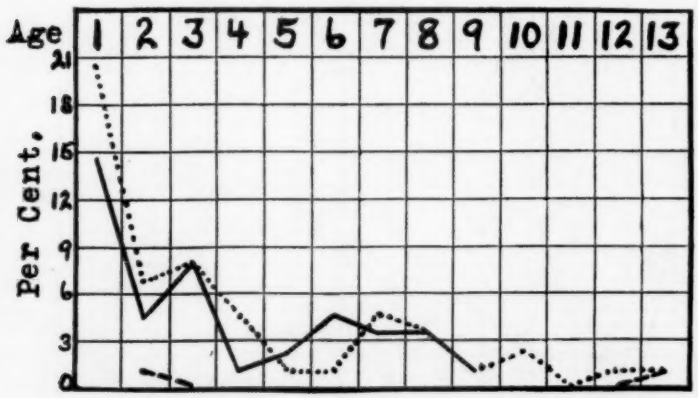

Chart 4.—The incidence of positive and negative antecedent family histories in children of the nonprotein sensitive group in relation to the age of onset of asthma.

per cent and positive in none. Thus, the total incidence of positive and negative family histories in this group was 45 and 55 per cent, respectively.

The curves in charts 2 and 4 are similar in contour.

Chart 5 shows the total incidence of the antecedent family history in relation to the age of onset of asthma in the children of the entire series. The family history was positive in 42 per cent (unilateral 39, bilateral 3) and negative in 58 per cent. The incidence of positive as well as negative family histories was largest when the onset of asthma occurred at 1 year (that is, including all infants from 3 months to 1 year) and as the children approached the age of 14 years, the incidence of positive and negative histories seemed to become progressively less.

Cooke and Vander Veer [37] maintained that when the inheritance of asthma is derived from both the maternal and the paternal sides

the period of greatest liability for allergy is the first five years; that when the inheritance is derived from either parent, the age of onset of asthma is between 10 and 15 years; in other words, they maintained that the more complete the inheritance, the earlier the manifestations of allergy will appear in the offspring. From a careful analysis of the data obtained in this series, I find that the facts do not harmonize with the conclusions deduced by Cooke and Vander Veer. In this series of 278 children a bilateral family history was obtained in only 2.9 per cent, which is in striking contrast to 24 per cent of the 56 comparable cases reported by Spain and Cooke.[39] It is also important to note that the incidence of unilateral family histories in this series is

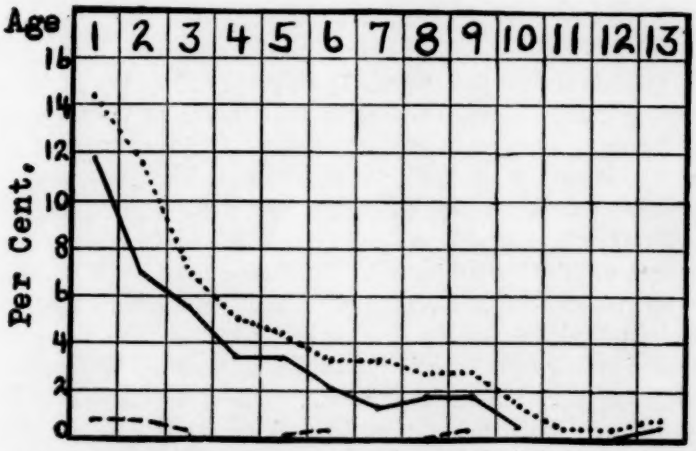

Chart 5.—The total incidence of positive and negative antecedent family histories in children of the entire series in relation to the age of onset of asthma.

largest with the onset of asthma during the first five years of life and that after 10 years of age the family history was positive in only 0.3 per cent.

COMMENT

Doerr,[40] who was the first to attempt classification of hypersensitiveness in the human being, believes now with Zinsser that the similarities between allergy and anaphylaxis are of more significance than the differences. Recent researches have largely diminished the significances of these differences which were formerly assumed by Coca and his co-workers to be of fundamental importance. Nevertheless, Coca still insists on the rigid separation of allergy (atopy) from anaphylaxis, basing his contention on the establishment of heredity as the sole determining factor. This extreme attitude, which discards many simi-

40. Doerr, R.: Die Idiosynkrasien, Handbuch der Inn. Med. **4**:448, 1926

larities in favor of a few differences, is illogical unless these differences can be shown to be fundamental. Zinsser did not believe that they are, and it seemed to him that such rigid separation is likely to impede understanding of the significance of many clinical manifestations.

Asthma is comparatively uncommon in the children of Central Europe. There, persons with asthma were tested with American protein extracts with little success. Later, extracts prepared in Holland by van Leeuwen,[41] in Denmark by Baagoe [42] and in Germany by Klewitz and Wigand [43] proved to be more potent than corresponding American extracts when used on patients residing in their respective countries. In spite of this, van Leeuwen found the incidence of allergic asthma in patients of all ages to be only 10 per cent. It is not surprising, then, if the clinician abroad views with suspicion the accuracy of the uniformly high incidences of allergic asthma, especially in children, reported in the American literature. These observations are of importance and help toward creating a better understanding of the subject of allergy and its relationship to the family history. I have observed with interest many persons of foreign birth whose antecedent family and past personal histories were negative to allergy, who after residing here for varying periods of time have developed symptoms of hypersensitiveness. This suggests acquired sensitization. The more uncommon sensitizations to such substances as ipecac, lycopodium and rhubarb that have caused asthma by inhalation in pharmacists, which I [44] have reported and sensitization to castor bean in a chemist, as reported by Bernton,[45] also strongly suggest acquired sensitization. I have seen hay-fever with asthma commence for the first time in patients ranging in age from 50 to 62 years, a period of life when for many reasons allergic disease is least expected to occur. How can this be logically explained, if not on the basis of acquired allergy?

Zinsser [11] succinctly summarized the important facts regarding this whole subject when he stated:

> It has already become apparent that many of the observations necessary for an understanding of these conditions cannot be made on animals. It is a peculi-

41. Van Leeuwen, W. Storm.: Allergic Diseases, Philadelphia, J. B. Lippincott Co., 1925.

42. Baagoe, K.: Dutch Preparations for Cutaneous Reactions; Comparative Skin Investigations with Danish and American Preparations, Hospitalstid. **69**:817 (Aug. 26) 1926.

43. Klewitz, F., and Wigand, R.: Die Hautimpfungen Beim Asthma Bronchiale, Klin. Wchnschr. **6**:784 (April 23) 1927.

44. Peshkin, M. M.: Ipecac Sensitization and Bronchial Asthma, J. A. M. A. **75**:1133 (Oct. 23) 1920; Bronchial Asthma and Other Allergic Manifestations in Pharmacists, ibid. **82**:1854 (June 7) 1924.

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arity of hypersensitiveness that identical inciting agents, by a probably identical mechanism, produce widely divergent effects in different species of animals, and many of the problems underlying the clinical manifestations of human hypersensitiveness can therefore be solved only by observation of the human being and by conservative experiment upon clinical material, so far as this may be safely done. . . Furthermore, the facts of hypersensitiveness, with the insurmountable similarity as to specificity, symptomatic complex, laws of desensitization, etc., teach us that such specific cellular reactiveness may be acquired against materials separated in regard to chemical structure as the simple iodides and the complex proteins and we are forced to conclude there is a common principle underlying all of them.

CONCLUSIONS

1. In a series of 285 children with asthma ranging in age from 3 months to 14 years, the antecedent family history to allergy in 278 instances was recorded as positive in 40 per cent of the patients of the protein sensitive and in 45 per cent of the nonprotein sensitive group, a total incidence of 42.5 per cent.

2. The onset of asthma is more frequent at 1 year than at any other age; and as the children approach the age of 10, the incidence seems to become progressively less. The incidence of onset of asthma during the first five years of life is approximately the same for the protein sensitive and nonprotein sensitive groups (about 75 per cent for each group). Patients with onset of asthma after 10 years of age are relatively uncommon.

The incidence of positive antecedent family histories of allergy in children of both the protein sensitive and nonprotein sensitive groups is larger with the onset of asthma at 1 year than at any other age. This also applies with reference to the incidence of negative family histories. As the children approach the age of 10 years, the incidence of positive as well as negative family histories which run parallel seems to become progressively less. The incidence of positive family histories in patients of the allergic and nonallergic groups with the onset of asthma during the first five years of life is 35 and 32 per cent, respectively, the negative family histories representing 43 and 40 per cent, respectively. No patients of the protein sensitive and only one of the nonprotein sensitive group show a positive family history after the age of 10.

3. There can be no question regarding the existence of a certain group of children in whom the "soil," "physiochemic make-up" or tendency to develop asthma is inherited. However, clinical and recent experimental data bring forcibly to light that there also exists another group of children in whom "allergic disease" is acquired. In the latter group, the lack of evidence pointing to the influence of heredity is striking.

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Case Reports

LIPOID HISTIOCYTOSIS (NIEMANN-PICK'S DISEASE)

WITH A REPORT OF A CASE DIAGNOSED DURING LIFE *

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At no period during life is an enlarged spleen so common an observation as in infancy. The majority of these splenic enlargements are secondary to or associated with an easily determined primary condition. There remains, however, a considerable group of obscure cases of splenomegaly in infancy, which are difficult of differentiation and which are frequently diagnosed only postmortem. There is, nevertheless, a splenomegaly occurring in lipoid histiocytosis (Niemann-Pick's disease) in which the diagnosis can definitely be made by means of splenic puncture and the determination of the blood lipoids. This is clearly shown in the following case.

REPORT OF CASE

History.—L. S., a white Jewish girl, aged 15 months, entered the hospital on April 4, 1927, with a complaint of vomiting and distended abdomen since the second month of life, and evidence of mental impairment, such as inability to sit up or to recognize parents. The condition was of three months' duration. The mother also complained that the child was restless and constipated.

The patient was the full term product of the seventh pregnancy. The parents and three older children were living and well. The child preceding this one had died at the age of 11 months. It had had a "large abdomen" since birth, the cause of which remained undiagnosed. The cause of its death was pneumonia. Two pregnancies terminated in abortions, each at three months. The patient's delivery was normal and spontaneous. The birth weight was 7 pounds (3.2 Kg.). Atelectasis was diagnosed soon after birth, but the child apparently was doing well until the age of 2 months.

The child was breast fed until it was 1 year old. It received complementary feedings from the second week to the second month, when this was discontinued because of vomiting. For the past several days before admission to the hospital, it had been given some vegetable soup and a milk mixture containing dextrimaltose.

The development of the child had been irregular. Its first tooth erupted at the age of 1 year; it sat up at the age of 8 months, and, according to the mother, talked at the same age. It had never stood alone or walked. For the past three

* Received for publication, April 11, 1928.

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months, the child had been in a hospital, and, as a result, the mother could give little of its recent history. She claimed that it had deteriorated mentally, acted queerly and had lost its ability to sit alone or to recognize its parents.

The medical history of the patient had been as follows. At birth atelectasis was diagnosed by the attending physician. The child seemed to have done well, nevertheless, until the age of 2 months when it began to vomit. This became progressively worse. When the child was 6 months of age, a physician found that it had an enlarged spleen and liver. Roentgen-ray therapy was begun; at first once weekly, and later, irregularly, twice weekly. After an initial improvement when the child appeared livelier, the vomiting became worse and was associated with loss of weight. For the past three months the patient has been in a hospital where it had otitis media; paracentesis was done twice.

Physical Examination.—Examination at the time of admission revealed a rather unusual appearing female infant. It had a peculiar complexion resembling the café au lait color found in congenitally syphilitic infants. Its cheeks in contrast were chapped and dusky red to an unequal degree; the condition was more marked on the side on which the patient was lying. The eyes were prominent, the eyelids puffy, and the left eye showed a lateral nystagmus. The mouth was usually open, revealing the red tip of the tongue, which was not enlarged or protruding. The child was constantly drooling. Its hair, eyebrows and lashes were long, sparse and fine.

The skin was soft and velvety. A seborrheic rash was present on the forehead and cheeks and behind the ears. From the middle of the thoracic region of the back to below the coccyx there were many larger and smaller mongolian spots. Two similar spots were present on the left leg. The upper part of the back and the forearms were covered with a fine down. The superficial veins were prominent.

There was no subcutaneous fat on the abdomen, and little on the thighs and gluteal regions, which were wrinkled, indicating, probably, a recent loss in weight. The sucking pads in the cheeks, however, were unusually well developed, resembling those found in premature infants. Turgor was markedly diminished; muscle tone was good.

The scalp was diffusely reddened throughout and was covered at intervals by greasy scales. The anterior fontanel was open.

The eyes were as described previously. There was no icteric discoloration of the sclerae. Pus issued from the inner canthi of both eyes. The ears and nose were normal. The mouth was open almost constantly. The upper and lower middle incisors had erupted. The tongue was coated, pointed, frequently extended or rolled around in the mouth. The tonsils and pharynx showed nothing abnormal. There was a marked fetor.

The neck presented a moderate enlargement, to the size of a bean of the posterior cervicals, bilaterally, and of the right submaxillary lymph glands. The thyroid was not palpable.

The chest was symmetrical. There was a slight increase in size of the costochondral junctions. The costal angle was acute, but there was moderate flaring of the costal margins. The lungs and heart were normal.

The abdomen was moderately distended. The lower part of the abdomen was boggy. Hard movable masses were present in the lower quadrants, especially on the left side.

The spleen was hard, firm and smooth, and it reached to about three finger-breadths below the costal margin. The splenic notch was distinctly palpable.

The liver was smooth and firm; it had a sharp, distinctly palpable edge, and extended about a handbreadth below the costal margin; otherwise the results of examination were essentially negative.

The tuberculin and repeated Wassermann and Kahn tests were negative.

The urine was normal.

The blood count showed: red blood cells, 2,820,000; hemoglobin, 50 per cent; color index, 90; white blood cells, 13,200; neutrophils, 58 per cent; lymphocytes, 33 per cent; monocytes, 7 per cent; eosinophils, 1 per cent; basophils, 1 per cent. Microcytosis was not present.

The weight at entrance was 6,000 Gm.; the temperature was 102.5 F.

Treatment and Course.—The child was placed on a diet consisting of milk, sugar, cereal, orange juice and egg-yolk. The weight curve was irregular, with gains or losses of as much as from 100 to 200 Gm. daily. The child vomited frequently and ruminated a great deal. The final weight was 5,900 Gm.

The temperature curve, too, was irregular. Subfebrile and febrile periods with fever as high as 103.5 F. occurred at intervals of several days.

The urine remained normal. The blood picture remained essentially unchanged.

A roentgenogram of the chest, skull and stomach was normal. The bones showed a mild degree of rickets.

The entrance diagnosis was: splenomegaly and hepatomegaly of unknown origin, malnutrition, seborrhea of the scalp, sweat rash of the body, mongolian spots and mental deficiency.

To arrive at the cause of the enlargement of the spleen and liver, I determined the coagulation and bleeding time and found these to be normal. The fragility of the red blood cells was found to be diminished.

On April 11, 1927, by eliminating the various other causes of splenomegaly and hepatomegaly at this age, and in view of the fact that the condition probably began in early infancy, I made a diagnosis of Gaucher's or Niemann-Pick's disease. The associated observations corresponding so closely to those described in Niemann-Pick's disease made me favor the latter diagnosis.

On April 22, 1927, a splenic puncture was performed. A fresh smear of the material obtained was examined by Dr. Jaffe, and the diagnosis of Niemann-Pick's disease was definitely established by the presence of typical foam cells.

The patient's general condition gradually became worse. On April 29, 1927, splenectomy was performed, and on April 30, the temperature rose to 108 F., and the child died.

Autopsy.—The spleen was removed by Dr. Hedblom and described by Dr. Jaffe.

The spleen removed at operation twenty hours before death weighed 122.9 Gm. Its dimensions were 10 by 6.5 by 3.5 cm. There were adhesions about the upper pole. The surface was smooth and of a pale yellowish gray. The cut surface was pale, homogeneous and of a pale yellowish red. Small round areas about 0.5 mm. in diameter, grayish and slightly translucent appeared at intervals (fig. 1).

Autopsy was performed by Dr. Jaffe one hour after death.

The skin was of a brownish gray and this color was most distinct over the abdomen. Slate gray-colored areas were symmetrically distributed on either side of the spine at the level of the seventh thoracic to the third lumbar vertebra. The diameter of the areas was from 2 to 3 cm. Larger patches were present over the first and second sacral vertebrae. The rest of the sacral and coccygeal area was covered by a roughly rectangular patch 6 by 3 cm. in diameter. Over the left leg posteriorly, two similar patches were present about 2 and 1 cm. in diameter.

Fig. 1.—Section through spleen showing actual size and color. Weight of spleen was 122.9 Gm. Cut surface is a pale, yellowish-red; the little red dots are malpighian bodies.

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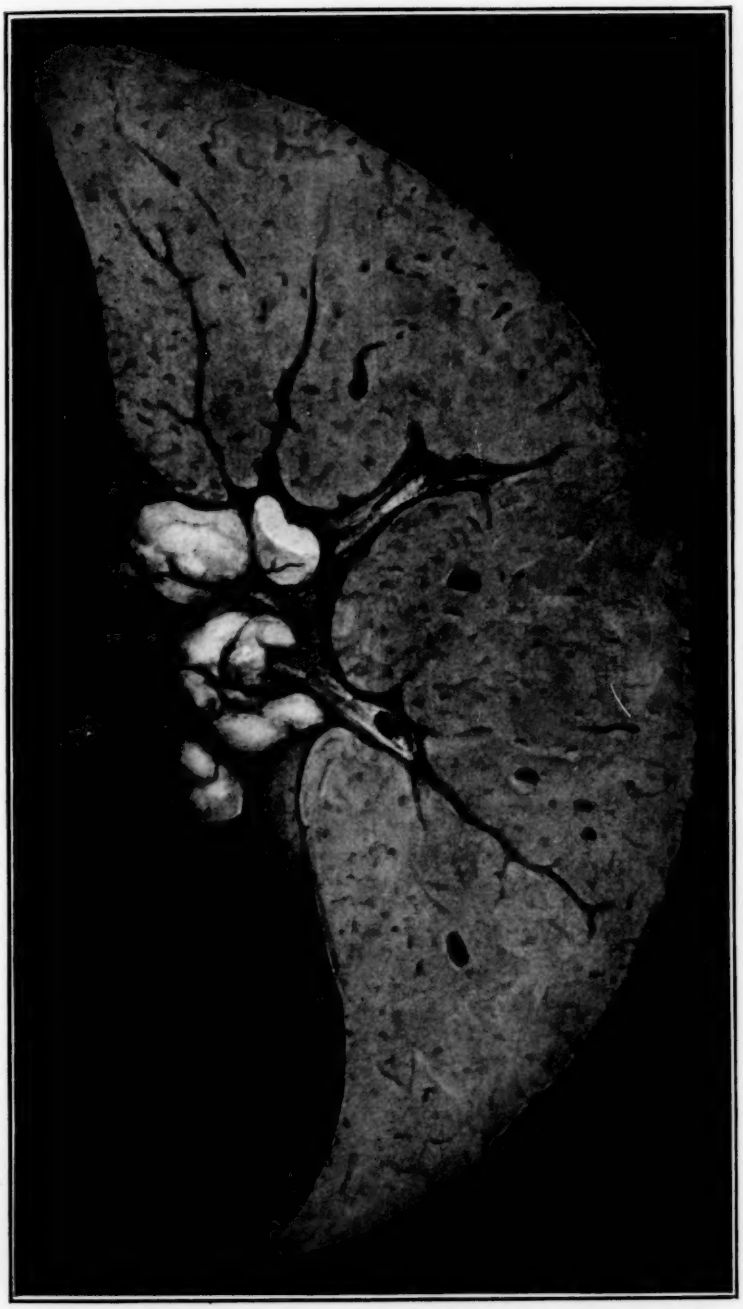

Fig. 2.—Section through liver showing actual size and color. Weight of liver was 583 Gm. The pale, claylike yellowish-gray color and the absence of acinar markings should be noted. The portal lymph glands are enlarged and yellow in color.

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The wound from the recent operation was situated in the left subcostal region.

The liver weighed 583 Gm. Its dimensions were 16 by 8 by 12 cm. The surface was smooth, and was of a pale yellowish gray, with indistinct reddish-gray areas. The consistency was firm. The cut surface was of a pale claylike yellowish gray without markings (fig. 2). The gallbladder was filled with thick, dark green bile.

The right kidney weighed 32 Gm. The capsule stripped easily leaving a smooth surface of a pale grayish red. The medulla was almost white. The cortical markings were indistinct. The left kidney weighed 31 Gm.; otherwise it was similar to the right.

The right suprarenal weighed 6.12 Gm. The cortex was from 1 to 1.5 mm. in thickness and was bright yellow. The internal zone was yellowish brown. The left suprarenal was similar; it weighed 6.17 Gm.

The stomach was distended and filled with a mucoid fluid. The mucosa was covered with mucus containing brownish shreds.

The plaques in the lower part of the ileum and the follicles were distinct. Above the ileocecal valve there was a large plaque 30 by 15 mm. of yellowish-white color. The surface of the plaques showed brainlike convolutions.

The pancreas weighed 14.72 Gm. It was firm, lobulated, and was reddish gray.

The lymph glands about the hilum of the liver were greatly enlarged from 2 to 2.5 cm. in diameter. They were soft, of medullary consistency, and bright yellow (fig. 2). The mesenteric glands were from 5 to 20 mm. in diameter, soft and reddish gray. The deep cervical glands were soft and bright yellow.

The thyroid weighed 3.5 Gm. It was firm, and a pale, reddish gray. Its cut surface was homogeneous, reddish gray and translucent.

The thymus weighed 4.95 Gm. and measured 6.5 by 3 by 1 cm. It was normal in shape, of a soft consistency and lobulated. The color was a claylike yellow.

The lungs were free. The pleura was thickened. The surface was grayish white, with slightly depressed reddish areas. The lungs floated in water, but felt firmer than normal. The cut surface was colorful. A system of peribronchial branched yellowish lines from 1 to 2 mm. in width separated deep red areas of lung tissue (fig. 3). These changes were most distinct in the lower lobe of the right lung.

The heart weighed 39 Gm. The thickness of the left ventricle was 8 mm.; that of the right, 2 mm. The myocardium was reddish gray.

The aorta above the valve was 30 mm. in width. Just about the valve, there was a flat yellowish-white plaque 9 by 7 mm. in size.

The bone marrow of the middle of the femur was a pale yellowish red and soft. In the ribs and sternum, it was a darker red.

Histologic Examination.—Under low power magnification, the splenic pulp appeared a mass of large round and pale stained cells. Besides the trabeculae, two structures were discernible; namely, the malpighian bodies and the sinuses. The malpighian bodies were large and showed distinct lighter centers. The sinuses were of varying width and usually contained a large number of cells.

The type cell of the splenic pulp may be described as follows: It was round or oval with a distinct membrane and a finely vacuolated cytoplasm. The vacuoles were round and of even size. They were separated by thin strands of cytoplasm and filled the entire cell body. There were a few cells in which large cavities were formed by fusion of the small vacuoles. The nuclei of the cells were round and were located in the center. The chromatin was scanty and was arranged in small granules, with one or two larger granules. These cells were densely packed together and reticulum fibers were not visible between them. There were few

other cells in the cords of the pulp; these were chiefly lymphocytes, larger lymphoid elements, single plasma cells and polymorphonuclear leukocytes.

The sinuses were lined by a low endothelium, which did not show any relation to the large foam cells of the cords. Although the nuclei were enlarged in places, the cytoplasm had not taken on the vacuolated appearance. The lumen contained many red cells, lymphocytes, single large round cells with a narrow rim of cytoplasm, and a large round pale stained nucleus with a large nucleolus. There were few free cells with a vacuolated protoplasm.

Fig. 3.—Section of lower lobe of the right lung. The peribronchial branched lines from 1 to 2 mm. in width separating darker areas of lung tissue should be noted.

The follicles had an outer zone composed of typical small lymphocytes, and a lighter central zone in which the same cells were present as were described in the pulp. Besides these, large lymphoid cells, with pale-stained nuclei and a scanty nonvacuolated cytoplasm were observed.

The veins of the trabeculae were filled with blood. Some of them showed a network of fibrin, with numerous leukocytes attached to the fibers.

In sections stained with sudan III, the cytoplasm of the foam cells assumed a pale, dirty, grayish-brown color, and distinct staining was not observed in the entire spleen. With nile blue sulphate, the cells remained practically unstained.

In Lorrain Smith-Dietrich sections, the contents of the vacuolated cells stained a deep bluish gray or black. The Caccio method brought out a differentiation in the staining qualities of the lipoids. The majority of the cells appeared a pale yellow. There were, however, cells, the cytoplasm of which showed a much more distinct coloration. It stained a bright orange yellow. These cells were most numerous in the center of the follicles and in their periphery. There were a few cells, the cytoplasm of which appeared in shades between the extremes of the pale pulp cells and the brightly stained cells of and about the follicles.

By Best's glycogen stain, a fine, reddish granulation was demonstrable in the trabeculae of the pulp. The granules lay about the connective tissue fibers.

The acini of the liver were composed of foam cells which were so densely packed together as to obscure the structure. The portal capillaries were barely visible. Close inspection revealed that there were two types of foam cells. The first type consisted of polyhedral cells which in places still showed some arrangement in cords. Their vacuoles were of medium size; large ones were rare. Between the vacuoles, there was a distinct network of cytoplasmic substance that stained pink in the hemalaun-eosin sections. In the peripheral part of these cells, the cytoplasm was usually more distinct. The nuclei were round and were located in the middle or near the periphery. Some showed a distinct chromatin structure and one or two nucleoli; others were more compact.

In sections stained with sudan III, many of these cells contained small or medium sized orange yellow droplets which accumulated near the margin of the cells. The majority of the vacuoles, however, remained unstained. In Lorrain Smith-Dietrich sections most of the vacuolar material assumed a deep gray or black color. The stained drops often showed a darker peripheral zone and a lighter center.

The second type of cell was larger and more irregular in shape. Their location in the portal capillaries was often distinct. They contained vacuoles which were smaller and more regular in size. Between these vacuoles there was a thin network of protoplasm. The nuclei were small and were usually located in or near the center. The outlines of the nuclei, which did not show a distinct structure, often appeared indented.

The two types of cells were put together like in a mosaic, but the first type predominated. As mentioned, the larger cells showed a relationship to the capillaries, from the endothelium of which they seemed to originate. There were smaller elements in which the vacuolization of the cytoplasm had not yet advanced to the extreme degree. These cells were still attached to the capillary wall. The large cells filled the lumen of the capillaries almost completely, and only a few red cells were found.

Similar cells also infiltrated the periportal connective tissue. Here, however, they appeared small. In the sheaths about the hepatic veins, the cells were large, and they often broke up the bundles of connective tissue to single fibrils.

In the large and finely vacuolated cells, a few of the droplets stained with sudan III. The majority of the droplets took a deep gray or black color in the Lorrain Smith-Dietrich sections.

Throughout the entire lymph gland, one found large, round and vacuolated cells. They lay singly or formed groups. The vacuoles which filled their bodies were usually small and regular in size. In places, the vacuoles fused together to make large holes, pushing the nucleus to one side of the cell. The vacuoles produced small deformities in the membranes of the nuclei. The nuclei had a loose network of chromatin granules. In the cells in which the vacuolization had not yet advanced to the extreme degree, the cytoplasm contained phagocytosed

material, such as granules and débris of shrunken nuclei, and single red cells. Even in the cells, the cytoplasm of which had been replaced by vacuoles, some débris of chromatin was found occasionally.

The vacuolated cells piled up in the marginal sinuses as well as in the medullary sinuses. They also formed groups in the centers of the follicles, resembling germinal centers. The latter groups contained, besides the foam cells, lymphoid elements without vacuolization, and free deeply stained granules. There were a number of mitotic figures in these areas, the chromosomes being short and the cytoplasm of the dividing cells being homogeneous. From these dividing cells elements developed with an ample cytoplasm and round nuclei, which often showed

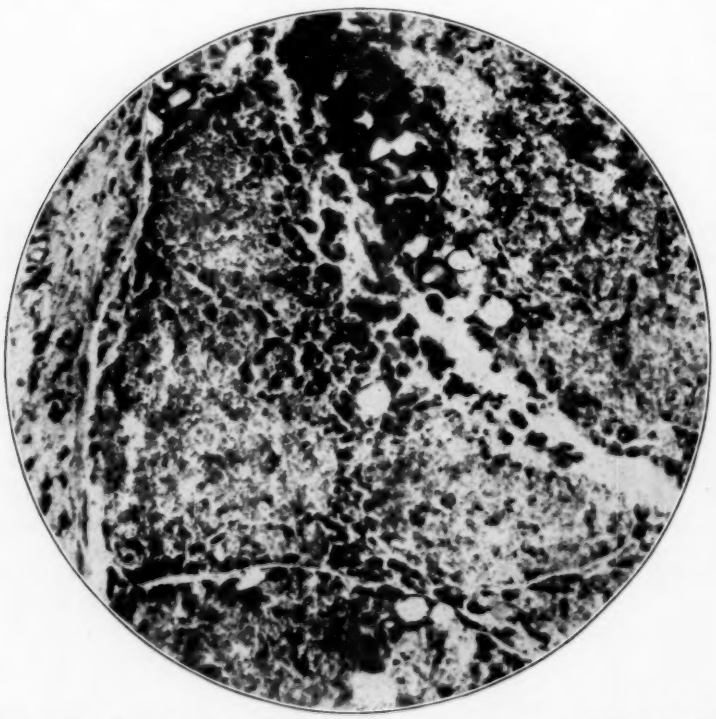

Fig. 4.—Section of lymph gland fixed in 10 per cent formaldehyde. In the upper half of the field a group of foam cells, transformed into large fat cells, is seen. Their contents, predominantly neutral fat and not phosphatides as in the other organs, are bright orange yellow in the stained preparation, appearing black in the photomicrograph. Frozen section; Sudan III hematoxylin; × 120.

a distinct acidophilic nucleolus. In the cytoplasm small droplets of lipoid material were seen.

The material which filled the vacuoles showed a much greater affinity for the sudan stain than that in the spleen or liver. Many of the cells were filled with bright orange yellow droplets. There were some cells in which these droplets were scanty; and finally, there were also cells the contents of which stained a faint yellow with sudan III. In the section stained by the Caccio method, much yellow colored material was seen. Some of the fat, however, did not take the Caccio stain.

The changes described were observed in all the glands examined, but they were most pronounced in the deep cervical glands and in the glands around the hilum of the liver. Here the lymphatic tissue was reduced to small islands of lymphocytes embedded in dense accumulations of the vacuolated cells. The fat droplets stained with sudan III showed a tendency to fuse to large single drops which filled the whole cell body, and these cells could not be distinguished from typical fat cells (fig. 4).

The capsule and the trabeculae of the glands were thickened, and, here too, a large number of fat-containing cells had piled up. These cells were usually flat, elongated or branched, and contained small granules.

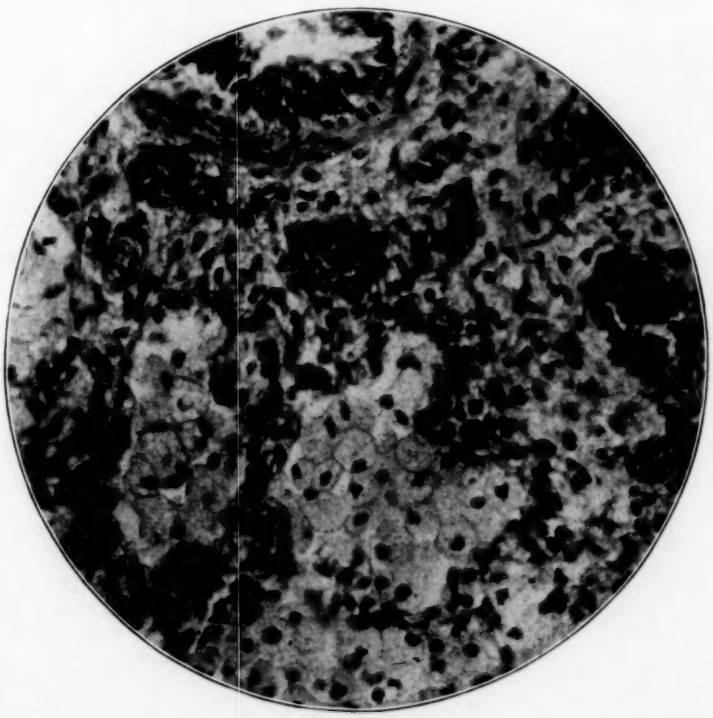

Fig. 5.—Section of lung. In the center are seen two alveoli filled with foam cells. These two alveoli are closely adjacent to a small bronchus; × 300.

In the lower lobe of the right lung, many alveoli were filled with foam cells. They lay so close to each other that solid pavement-like structures resulted (fig. 5). Many cells contained from one to five nuclei. Some of the cells had engulfed red blood corpuscles. The erythrocytes appeared crenated, the vacuoles filling the depressions on their surface. When these cells were in the process of formation, their origin from the alveolar septums was distinct. They seemed to grow into the alveoli from the tissue about the alveolar capillaries.

Fat could not be demonstrated by the sudan III stain in the foam cells. The Lorain Smith-Dietrich method brought out a deep gray or black granulation in the small vacuoles. The foam cells stained a pale yellow in the sections stained by the Caccio method. Some of the cells took a deep orange yellow coloration. The most

distinct staining was found in flat and branched cells in the connective tissue about the larger blood vessels. These cells were packed with deep orange yellow granules. Fat was not present in the epithelium of the bronchi. Coal dust was present in the foam cells.

The thymus consisted chiefly of the large foam cells described in the other organs. Only a few dark nucleated thymus cells were found between them. In some places, the thymus cells were more numerous and occupied the peripheral zone of the lobule. The lobules were separated by much fibrillar connective tissue. The septums contained a large number of vacuolated cells which separated the single fibrils of the connective tissue. The foam cells seemed to proliferate from

Fig. 6.—Section of thymus. Groups of foam cells are present in the medulla and are less numerous in the cortex; × 90.

the interlobar septums into the lobules (fig. 6). Hassall's bodies were present only in those places in which some thymus tissue was left. Eosinophil granulated cells were absent.

Most of the material in the foam cells stained a deep gray or black in the Lorrain Smith-Dietrich sections, and the Caccio stain brought out a great many orange colored granules or droplets. In some of the cells, all the fat was stained with the Caccio stain.

The bone marrow was cellular, but everywhere single or groups of fat cells were found. There were many round or oval cells with round nuclei and with a fine or coarse granulation. The latter stained a bright brick red with eosin. There were small groups of oval or round cells with a deeply stained, basophilic

cytoplasm and with large nuclei that contained a dense and coarse network of chromatin. Many dark nucleated oxyphilic cells with segmentation of the nuclei were observed. Polymorphonuclear leukocytes were less numerous. One found many bone marrow giant cells, many of which had pyknotic nuclei. There were many erythrocytes. In every field, a number of foam cells could be seen. Their cytoplasm was finely vacuolated, and in some of the cells engulfed red cells were visible (fig. 7). The capillary endothelium did not show any relation to the foam cells.

The cells of the cortex of the suprarenal contained small lipoid granules. The medulla was replaced to a large extent by large, round or oval cells, with a finely

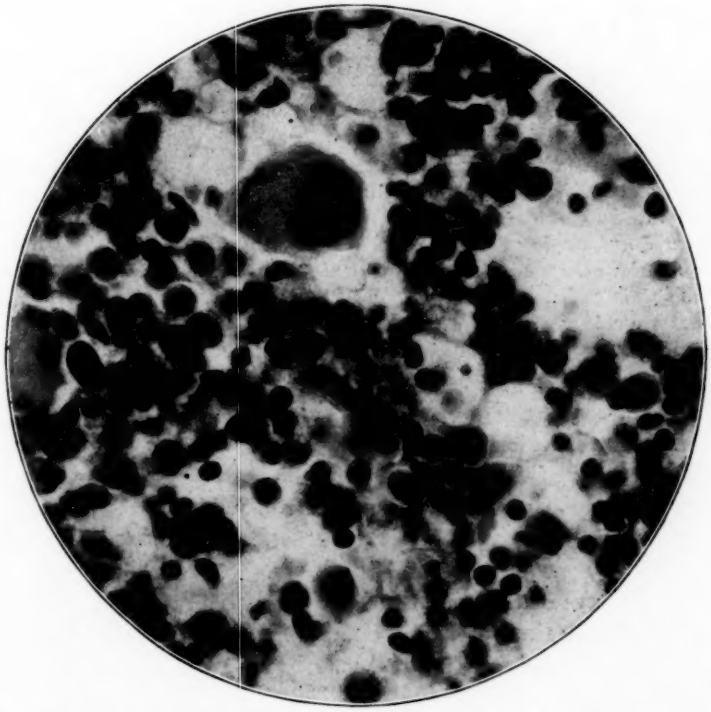

Fig. 7.—Section of bone marrow. Approximately in the center, a foam cell with a phagocyted erythrocyte is seen. The nucleus of the cell is indistinct. The two dark nuclei are located above the cell. Above the center is a bone marrow giant cell with pyknotic nucleus. Groups of normoblasts and eosinophil myelocytes are found. Foam cells are seen throughout the field; × 625.

vacuolated cytoplasm and small dark nuclei. These cells formed alveoli which seemed to be surrounded by a thin capsule of connective tissue. Some of the cells lay free but did not show a tendency to invade the corticals. Only a little medullary tissue remained.

In the sections stained with sudan III, one could distinguish two forms of foam cells. Usually one form predominated in each alveolus. There were alveoli chiefly composed of cells, the contents of which stained a bright orange yellow with the sudan. The droplets were small. In other alveoli, the majority of the

foam cells remained unstained. In the Lorrain Smith-Dietrich sections all the granules, those in the cortical cells and those in the foam cells of the medulla, took a deep gray color; while the Caccio stain brought out only a few small granules.

The Peyer's plaques in the ileum showed distinct germinal centers, which appeared loose. A few round lymphoid cells with round nuclei, and single larger elements with a vacuolated cytoplasm were present. The latter type of cells was found also in other parts of the lymphatic tissue, and they became most numerous in the basal parts of the plaques near the muscularis, where they formed groups.

In the epithelial cells of the convoluted tubuli of the kidney, smaller and larger fat droplets were found. The glomeruli appeared normal, and changes were not found in the interstitial connective tissue. Foam cells were scarce and were restricted to a few glomerular tufts. They seemed to be located in the lumen of the tufts, filling it more or less completely.

The vesicles of the thyroid were of regular size and shape. Their lining was low cuboidal. They were filled with homogeneous oxyphilic colloid. There were a few small lipoid granules in the epithelium. The stroma was not increased. In the Mallory sections the colloid stained uniformly a bright brick red.

The pancreas did not present any abnormalities. The islands were well developed and distinctly separated from the acinar part. Fat was not present in the epithelial cells of the acini, islands or ducts. In the connective tissue about the larger ducts, single cells filled with fat granules were found. The cells were of various shapes, round, oval or elongated. The fat they contained stained as well with plain sudan III as with the Caccio method.

There were large masses of all the different kinds of nucleated blood cells in a blood clot from the right ventricle. Foam cells could not be found.

GENERAL CHARACTERISTICS

A survey of the cases observed up to the present time reveals the disease to be more frequent among girls than among boys, the ratio being 8:2. It also appears to affect predominantly, if not exclusively, children of eastern European Jewish descent. The two cases of Knox, Wahl and Schmeisser [1] occurred in sisters. A sister of the patient in Siegmund's [2] case died during the first year of life with a large liver and spleen. I also obtained a vague history of a child preceding my patient, who died at 11 months of age and who had a large abdomen, the cause of which remained undiagnosed.

The disease is possibly congenital; it begins no later than during the first months of life. The clinical pictures in all the cases were remarkably similar. The patients frequently appear mentally defective. The expression may be mongoloid as in Niemann's [3] and Bloom's [4] cases or

1. Knox, J. H. M.; Wahl, H. R., and Schmeisser, H. C.: Gaucher's Disease, a Report of Two Cases in Infants, Bull. Johns Hopkins Hosp. **26**:60, 1915; **27**:1, 1916.

2. Siegmund: Lipoidzellen hyperplasie der Milz und Splenomegalie Gaucher, Verhandl. d. deutsch. path. Gesellsch. **18**:59, 1921.

3. Niemann, Albert: Ein unbekanntes Krankheitsbild, Jahrb. f. Kinderh. **79**:1, 1914.

4. Bloom, William: Splenomegaly (Type Gaucher) and Lipoid-Histiocytosis (Type Niemann), Am. J. Path. **1**:595, 1925.

amaurotic-idiotic as in Knox, Wahl and Schmeisser,[1] and in Hamburger's [5] cases. The patient's expression in my case was more mongoloid than otherwise, but not typically so. The skin, especially of the exposed portions, is brownish or grayish yellow. There is a tendency to edema of the eyelids, ankles and feet or mild ascites. Most striking is the enlargement of the spleen, liver and lymph glands, of varying degree, with the splenic enlargement usually marked.

The children do not do well. Their nutritional condition is not good. They are markedly retarded in their physical and psychic development, and they usually die before the eighteenth month of life of exhaustion or secondary infection.

The urine is normal. The blood shows a moderate leukocytosis. The blood may be lipemic cloudy (Hamburger,[5] Schiff [6]). In the case herein reported, the first in which a fractional determination of the blood lipoids was made, the results of examination of the blood are shown in the accompanying table.

Results of Determination of the Blood Lipoids Per Hundred Cubic Centimeters of Blood

		Normal	Per Cent Increase
Phosphatides	24 mg.	12-14 mg.	70
Cholesterol	231 mg.	140-170 mg.	35
Total fatty acids	560 mg.	290-420 mg.	33

The condition can be suspected in cases of splenomegaly in infancy showing the clinical picture described. It can definitely be diagnosed by finding the typical cells in the material obtained by splenic puncture, and possibly by the changes in the blood lipoids.

The disease appears to be one of disturbed lipoid metabolism. The lipoids appear to be deposited in the reticulo-endothelial cells of the spleen, liver, lymph glands and bone marrow, and also of the thymus and suprarenals. Probably only when the capacity of these organs has been exhausted does deposition of lipoids occur also in the specific parenchymal cells of the various organs—the liver, kidney and myocardium.

In a recent publication, Pick [7] states that after the storage capacity for lipoids of the histiocytes has been exhausted, they will be stored in

5. Hamburger, R., cited by Pick: Ergebn. d. inn. Med. u. Kinderh. **29**:519, 1926.

6. Schiff, E.: Im Leben diagnostizierte lipoidzellige Splenohepatomegalie (Typus Niemann-Pick) bei einem 17 Monate alten Knaben, Jahrb. f. Kinderh. **112**:1, 1926.

7. Pick, L.: Ueber die lipoidzellige Splenohepatomegalie, Typus Niemann-Pick als Stoffwechselerkrankung, Med. Klin. **23**:1483, 1927.

other cells. He has found phagocytized lipoids in cartilage cells, smooth and striated muscle, in ganglion, glia and Schwann sheath cells, and also in the epithelial cells of the liver, alveoli of the lung, bronchi, mucous glands of the trachea, thyroid, salivary glands, kidneys, suprarenals, pancreas, ovary, hypophysis and other organs.

As a result of the study of the brain in Hamburger's case, Pick and Bielschowsky suggest an intimate relationship between Niemann-Pick's disease and amaurotic family idiocy. They believe that both conditions are manifestations in varying degrees and distribution of the same, or of a similar, disturbance in lipoid metabolism.

Pathologically, one finds the picture resulting from the extensive deposition of lipoids in the cells of the various organs. The detailed macroscopic and microscopic pictures of the disease can be found in the account of the observations found at autopsy in my case, as well as in the descriptions by Pick [8] and by Bloom.[4]

In the case herein reported, the following interesting features were presented. Histologically, variations in the composition of the lipoid mixtures in the different organs were noted. While phosphatides predominated in most of the organs involved, namely, the spleen, liver, thymus and lung, the abdominal lymph glands showed a preponderance of neutral fats. This would explain their peculiar bright yellow color. The histologic observations correspond with those of the blood chemistry. All of the lipoid fractions of the blood showed a distinct increase above the normal, but to an unequal degree. The lipoid phosphorus fractions showed the greatest increase of 70 per cent. The fatty acids and cholesterol showed an increase of 33 and 35 per cent, respectively.

I was also able to observe that in the lung the foam cells originated from the mesenchymatous cells around the alveolar capillaries, cells identical with the septal cells of Maximow and Lang. In the liver, they originated from the Kupffer and the adventitial cells; in the spleen, from the reticulum cells. In the thymus, the origin of the foam cells seemed to be not from the ectodermal reticulum cells but from mesenchymatous cells around the smaller blood vessels, especially in the interlobular septums.

NOTE.—The chemical examination of the organs removed at autopsy is being made by Mr. R. MacFate of the Department of Chemistry, and the observations will be reported when completed.

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8. Pick, Ludwig: Der Morbus Gaucher und die ihm ähnlichen Erkrankungen, Ergebn. d. inn. Med. u. Kinderh. **29**:519, 1926.

CONGENITAL HEART BLOCK

REPORT OF AN ADDITIONAL CASE, WITH REVIEW OF LITERATURE *

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AND
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Marked bradycardia in persons in middle or later life was first described by Morgagni in 1761. It is only in recent years, however, that accounts of the condition in children have appeared. In nineteen instances, the bradycardia apparently was due to congenital heart block. This disorder in infants is sufficiently rare to warrant the recording of an additional case.

It is evident that the diagnosis of congenital heart block can rarely be proved because of the lack of exact observations on fetal heart rates. This condition, however, must be seriously considered in a child with a slow pulse rate when a history of acquired disease, such as diphtheria, rheumatic fever, syphilis or severe pyogenic infection is not obtained. The accepted cases were proved by electrocardiograms or pulse tracings. Graphic proof of heart block was delayed until later years in several instances, but in these a history of some circulatory disorder, accompanied by syncope and a slow pulse rate, makes the diagnosis probable.

REVIEW OF THE LITERATURE

As far as we can determine, Schuster,[1] in 1896, was the first to mention the occurrence of bradycardia early in childhood. He published the report of a case of rheumatic fever in a child, aged 4, with a pulse rate of 35 which returned to normal with recovery. In 1901, Morquio [2] described five brothers, each of whom developed a slow pulse rate at the age of 4, with frequent attacks of syncope and convulsions from trivial causes. Four of them died during attacks before their ninth year, one under his observation, but autopsy did not reveal an explanation. As described, their pulse rates were more suggestive of fibrillation, for they varied in rate and volume and were irregular at all times. He also mentioned the case of a child, aged 4, with probable congenital heart block who was brought to his clinic by Scoseria. The patient showed a regular pulse rate of 40, and a history was given of

* Received for publication, Jan. 30, 1928.

* From the Departments of Medicine and Pediatrics of Western Reserve University Medical School at City Hospital.

1. Schuster: Deutsche. med. Wchnschr., July-Dec., 1896.
2. Morquio: Arch. de méd. d. enf. **4**:467, 1901.

syncopal attacks beginning at the age of 9 months. A diagnosis of interventricular septum defect was made because of an intense diffuse systolic murmur at the base, even though cyanosis was not present.

Von Starck,[3] in 1903, recorded a case of a boy, aged 5, with a history of frequent attacks of bronchitis accompanied by syncope and a slow pulse rate of from 28 to 40. Zahorsky,[4] in 1915, described the case of a girl, aged 15 months, with a pulse rate of 54 regardless of posture or activity. There was a systolic murmur over the precordium, thought to be due to congenital heart disease. In Gill's [5] case the patient showed a slow pulse rate (49 per minute) at the age of 3. Graphic proof of block in these cases was not obtained.

Brief descriptions of the accepted cases are given in the table. While the patient in van den Heuvel's [6] case was not seen until the age of 23, at which time the pulse rate was 34, she suffered syncopal attacks which began when she was 2 years of age. The diagnosis of complete heart block and defect of the septum was made. In the case of Barbier, Lebee and Mouquin [7] the patient was first seen at the age of 14. Electrocardiograms showed complete heart block, and a septum defect was suspected. The patient described by Bass [8] was 13 years of age when bradycardia was first noticed. In all the other cases the patients showed bradycardia before the age of 9. White, Eustis and Kerr [9] described a boy, aged 6, with congenital syphilis and complete heart block, but they considered this a doubtful case because a normal heart was described at the age of 5. The same authors presented the first observation of block in a fetal heart which was slow and irregular. On the second day after birth the pulse rate varied from regular at 80 to bigeminy at 105, trigeminy at 120, and regular at 160. This patient, a Mongolian idiot, was considered to have a paroxysmal congenital heart block with patent ductus arteriosus and ventricular septum defect. An electrocardiogram which was made when the child was 4 days old showed a rhythm varying from a normal mechanism to 3-2 and 2-1 heart block.

In 1921, Smith [10] described an otherwise healthy man, aged 20, who gave a history of syncope between the ages of 3 and 9 years. He was

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3. Von Starck: Monatschr. f. Kinderh. **2**:11-15, 1903.

4. Zahorsky: Interstate M. J. **22**:57, 1915.

5. Gill: Australasian M. Gaz. **30**:1 (Jan. 20) 1911.

6. van den Heuvel: Proefschrift aan de Rijks Universitait, Groenigen, Dec., 1908.

7. Barbier, Lebee and Mouquin: Soc. de Ped., Jan. 17, 1922; reviewed in Arch. d. mal. du coeur **15**:171, 1922.

8. Bass, M. H.: Heart block and Congenital Heart Disease in Childhood, J. A. M. A. **70**:287 (Feb. 2) 1918.

9. White, P. D.; Eustis, R. S., and Kerr, W. J.: Congenital Heart Block, Am. J. Dis. Child. **22**:299 (Sept.) 1921.

10. Smith, S. C.: High Grade Heart Block, J. A. M. A. **76**:17 (Jan. 1) 1921.

Data of Cases Reported by Different Authors

No.	Author	Sex	Age	Symptoms	Other Diagnosis	Auricular Rate	Ventricular Rate	Murmurs
1.	van den Heuvel [6]	F	23 yr.	Syncope 2 years; slow pulse 15 years	Interventricular septum defect	128	34-38	Systolic
2.	Fulton, Judson and Norris: Am. J. M. Sc. **140**: 339, 1910	M	2½ yr.	Slow pulse at 7 days...	? of septum defect.....	...	42	Systolic
3.	D'Espine and Cottin [15]	M	8 yr.	Syncope at 8 years.....	Congenital syphilis	104	20-32	Extra systolic
4.	Whipham: Brit. J. Child. Dis. **12**: 321, 1915	F	12 yr.	Slow pulse at 6 years; precordial pain	Interventricular septum defect	75	40-64	Systolic and slight diastolic
5.	Whipham	F	1½ yr.	None	Interventricular septum defect	...	48-53	Systolic
6.	Bass [8]	M	15 yr.	Dyspnea and palpitation	Congenital heart	107	40-44	Systolic
7.	Gorter: Nederl. Maandschr. v. Verlosk., 1919	M	6 mo.	Pulse rate 72 six hours after birth	.....	150	68-72	None
8.	Carter and Howland: Bull. Johns Hopkins Hosp. **31**: 351, 1920	F	10 yr.	Slow pulse at 3 years	Interventricular septum defect	...	34	Systolic
9.	Rosenson: Arch. Pediat. **39**: 567, 1922	F	11 yr.	Heart pain at 7 years	Congenital opening between aorta and pulmonary artery	100	44-60	Systolic and diastolic
10.	Calandre [11]	M	21 yr.	None	.....	70	45	None
11.	Smith [10]	M	20 yr.	Syncope 3 to 9 years...	.....	...	40	None
12.	White, Eustis and Kerr [9]	F	4 da.	Prenatal slow pulse....	Septum defect and ductus arteriosis	150	80-160	Systolic
13.	Barbier, Lebee and Mouquin [7]	..	14 yr.	Dyspnea.....	Interventricular septum defect	...	.....	
14.	Frias: Arch. españ. de pediat., August, 1922	F	5 yr.	Slow pulse at 4 years	.....	110	46	None
15.	Romberg and White: Boston M. & S. J. **190**: 591 (April) 1924	F	9 mo.	None	Interventricular septum defect	160	60-70	Systolic and diastolic
16.	Wilson and Grant [12]	F	14 mo.	Blue baby.....	Congenital pulmonary stenosis and septum defect	...	60-70	Systolic
17.	Gibson: Am. J. Dis. Child. **34**: 1090 (Dec.) 1927	F	9 yr.	None.....	Interventricular septum defect	...	50	Systolic
18.	Aldrich [13]	F	4 yr.	None.....	Congenital heart	...	45	Not mentioned
19.	McIntosh [14]	F	7 mo.	None.....	Interventricular septum defect	136	60-64	Systolic
20.	Our case	M	13 mo.	None.....	Interventricular septum defect	136	47	Systolic

in good health, able to play baseball and frequently danced far into the night without discomfort. The electrocardiogram showed complete auriculoventricular dissociation with a pulse rate of about 40; but a normal mechanism with a rate of 58 was established for short periods by forced expiration. Evidence of valvular or developmental lesion of the heart was lacking. Congenital origin of the block was not suggested by the author. The case of a man, aged 21, who was apparently healthy and able to withstand strenuous exercise without discomfort, was described by Calandre.[11] There was no history of vertigo, attacks of fainting or circulatory disorder, though the patient was known to have had a slow pulse rate of about 40 since birth. Under observation the pulse rate varied from 37 to 52, the latter occurring with fever. The heart was apparently normal except for complete block proved by electrocardiogram. During a period of complete repose, however, a normal mechanism was recorded with a slow rate. The P-R interval was under 0.2 second. Amyl nitrite and atropine increased the auricular rate without altering the ventricular rate.

Wilson and Grant [12] presented the only case showing marked cyanosis or clubbing of the fingers or toes. This also is the only case reported with postmortem examination. The child, aged 14 months, had had a systolic murmur and thrill. Electrocardiograms showed 2 to 1 heart block, and a diagnosis was made of congenital interventricular septum defect and pulmonary stenosis. Autopsy disclosed a cor biatriatum triloculare with obliteration of the pulmonary artery. The auriculoventricular node and bundle of His, identified and followed into the ventricular musculature, were surrounded and separated by strands of fibrous tissue and numerous small blood vessels.

Death is recorded in only two other cases, in neither of which the patient was examined postmortem. The patient described by Aldrich [13] died suddenly at 13 years of age while apparently in good health. In the case of McIntosh,[14] death occurred after eight months of infection independent of the heart condition.

REPORT OF AUTHORS' CASE

History.—Albert R., a boy, aged 13 months, was admitted to City Hospital on Jan. 31, 1927, because of malnutrition. The family history did not give any evidence of tuberculosis, syphilis, alcoholism, cardiac disorders or other chronic diseases. The father and mother were living and well, and the mother's Wassermann reaction was negative. Two previous pregnancies had terminated in spon-

11. Calandre: Arch. de cardiol. y hematol. **2**:225 (June) 1921.

12. Wilson and Grant: Heart **12**:271 (March) 1926.

13. Aldrich, in discussion on Gibson: Heart Block, abstr. Am. J. Dis. Child. **34**:1090 (Dec.) 1927.

14. McIntosh, R.: Congenital Heart Block, Am. J. Dis Child. **34**:965 (Dec.) 1927.

taneous miscarriages without known cause after a gestation of five months. The past history revealed that the child was delivered normally and weighed 6 pounds (2.7 Kg.) at birth. He had had artificial food since birth, including cod liver oil and orange juice. No history of infectious disease or other illness was obtainable. It may be especially emphasized that there had been no cyanosis, syncope, dyspnea or convulsive seizures.

Physical Examination.—The patient was small and undernourished and weighed 5,275 Gm. He was able to sit up alone, but he usually lay quietly in bed. The skin was of average color and texture. The subcutaneous fat was reduced in amount. The fingers did not show any cyanosis or clubbing. A definite Harrison's groove with slight beading of the costochondral junctions was noted. The pulse rate was slow, about 40 a minute, but regular and full and without disparity between radial and apical rates. There was a small circumscribed area of pre-

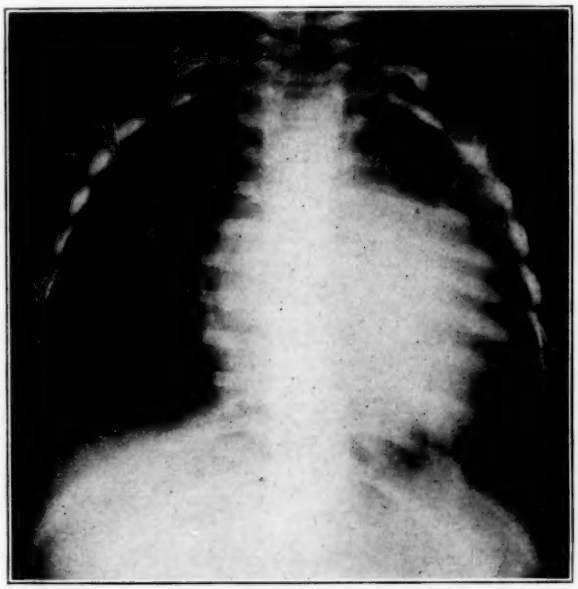

Fig. 1.—Roentgenogram of the heart taken at a distance of 7 feet.

cordial impulse just outside the nipple line in the fifth intercostal space. A distinct systolic thrill was palpaple to the left of the sternum. The left border of the heart extended 1.5 cm. outside the left nipple line and the right border from 0.5 to 1 cm. to the right of the right sternal margin. A loud, harsh systolic murmur was heard over the entire precordium, but was loudest along the left border of the sternum at the third interspace and was transmitted throughout the entire chest. The pulmonic second sound was definitely accentuated. Auricular sounds were occasionally heard at the base of the heart independent of the ventricular sounds.

Laboratory Observations.—The urine was normal. The blood counts showed 6,025,000 red cells and 6,600 white cells; hemoglobin was 80 per cent (Tallquist). Intradermal tuberculin reactions were negative in dilutions of 1:1,000 and 1:100. The Wassermann reaction of the blood was also negative. A roentgeno-

gram (7 ft. heart plate) and fluoroscopic examination by Dr. David Steel showed a globular heart increased in all diameters but most markedly to the left and vigorous pulsations in the region of the left ventricle and pulmonary artery. Auricular contractions were more rapid than the ventricular. The electrocardiogram showed complete atrioventricular block with marked right ventricular

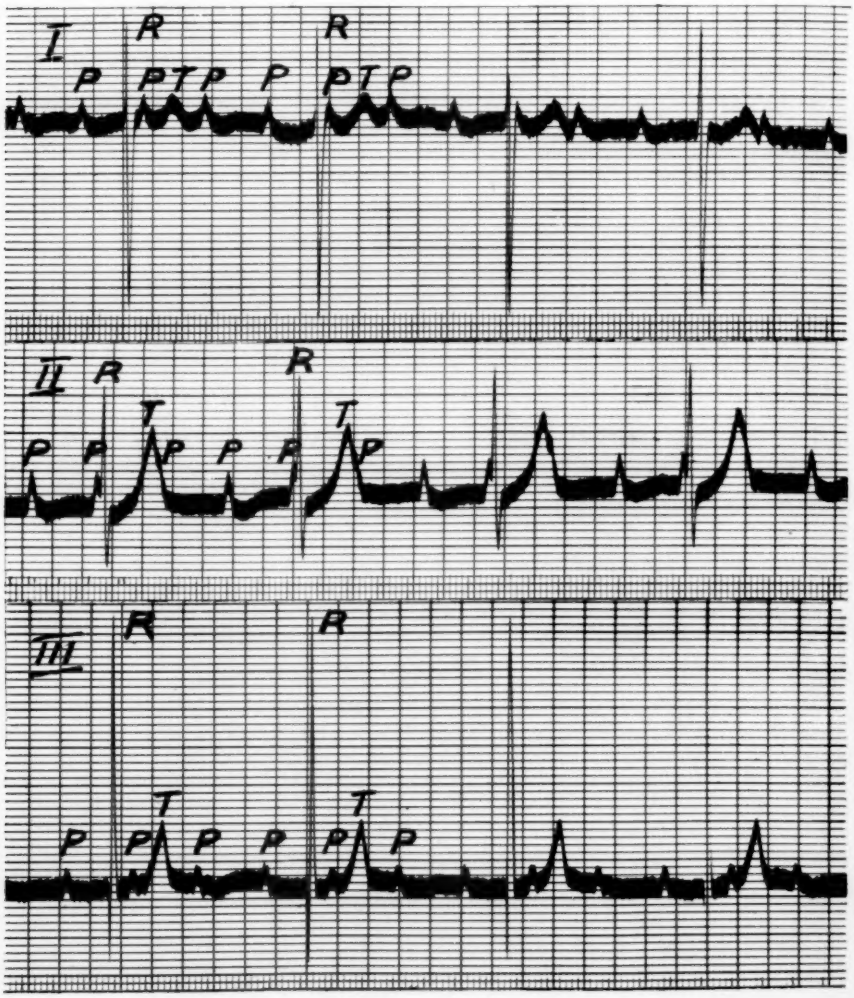

Fig. 2.—Electrocardiographic tracing, three leads, showing complete heart block and marked right ventricular preponderance; ventricular rate 46, auricular rate 144.

preponderance. The auricular rate was 125 per minute and the ventricular rate was 45; both were regular.

Clinical Course.—Frequent electrocardiograms consistently showed complete heart block and marked right ventricular preponderance with a ventricular rate under 50. During an attack of bronchopneumonia, the pulse rate clinically varied

from 55 to 72. After recovery, the pulse rate returned to its former rate. The auricular rate ordinarily ranged between 125 and 144. After the marked effect of atropine, the auricular rate rose to 150, while the ventricular rate remained unchanged. During seven weeks in the hospital, the patient gained 765 Gm.; other changes were not observed.

The patient was last seen on Dec. 28, 1927, eleven months after admission. Changes were not noted by physical examination, electrocardiogram or roent-

COMMENT

There is a notable lack of uniformity of symptoms in this group of cases that had so much in common. The condition caused little concern in many of the patients, and in several instances the heart block was an incidental observation. A history of syncope was found in three cases; this was transitory in two. Precordial pain on exertion was the complaint of two patients, as was also dyspnea and palpitation. Cyanosis and clubbing of the extremities were present in one case, while slight cyanosis was recorded in three other instances.

The association of congenital heart block with other cardiac anomalies and disease is striking. Developmental septal defects occurred in thirteen cases. Congenital heart block without further description was mentioned twice. D'Espine and Cottin [15] suspected that their patient had congenital syphilitic involvement of the conduction system because of a positive Wassermann reaction. Associated heart disease was not mentioned in only four cases.

The degree of block varied. It was complete in sixteen cases (cases 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 13, 14, 15, 17, 19 and 20). There was alternating complete and 2-1 block in case 5, only 3-1 block in case 18, 2-1 in case 16, and paroxysmal, varying from 4-1 to normal mechanism in case 12. The degree of block was not mentioned in case 14. There was a wide variation in pulse rates, though in individual cases the pulse was less labile than normal. The widest variation in any case with complete block ranged from 40 to 64. The slowest pulse rate was 20, and in eleven cases the patients had pulse rates under 50 at all times. The fact that the block was so often complete suggests that in some of these cases developmental lesions of the conduction system itself may be responsible for this condition. The lack of more serious complaints in view of such circulatory disorder is surprising. The disease is apparently well borne during early life. Nothing can be said about prognosis, as only three deaths are recorded in this series.

CONCLUSIONS

1. The reports of nineteen instances of congenital heart block in the literature are reviewed, and an additional case is presented.

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15. D'Espine and Cottin: Bull. Acad. de méd., Paris **74**:292, 1915.

2. A lack of serious complaint in view of marked circulatory disorder in this condition is noted.

3. Complete heart block in many of these cases may have been due to a congenital defect of the conduction system.

4. The prognosis in individual cases is uncertain, though the disease seems to be well tolerated in early life.

Progress in Pediatrics

PREVENTION OF MEASLES *

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An outbreak of measles is perhaps, with the exception of smallpox, the most dreaded complication that occurs in a pediatric institution. Measles may appear in the institution at any time and may spread in spite of most careful isolation. The customary methods of prophylaxis are not always effective, and the literature during the past ten years bears testimony to the seriousness of the problem. In 1926, the total mortality of measles in continental United States was reported as 8,607 with a mortality rate of 8.2 per hundred thousand of the estimated population.[1] Any practicable method of prevention which can be made generally available should be given an open reception.

The use of human convalescent measles serum and whole blood was probably first advocated by Nicolle and Conseil [2] in the literature in 1918. In 1919, Richardson and Connor [3] inoculated three children with measles virus and simultaneously injected convalescent serum. One patient developed a slight rash and transient fever; the other two did not have any reaction. In the same year Terrien [4] injected whole blood from a brother who was six months convalescent, with favorable results in the treatment of a patient with malignant rubeola. Degkwitz [5] published his first results in 1920, and since then he has made an intensive study of the problems.[6] Some of the earlier literature was reviewed by Zingher.[7] The following reports, however, had appeared before

* Received for publication, April 12, 1928.
* Read before the Milwaukee County Medical Society, April 13, 1928.
* From the Milwaukee Children's Hospital.

1. U. S. Public Health Rep., Jan. 6, 1928, vol. 43.

2. Nicolle, C., and Conseil, E.: Bull. et mém. Soc. méd. d. hôp. de Paris **42**:336, 1918.

3. Richardson, D. L., and Connor, H. J.: Immunization against Measles, J. A. M. A. **72**:1046 (April 12) 1919.

4. Terrien, E.: Bull. et mém. Soc. méd. d. hôp. de Paris **43**:1134 (Dec. 26) 1919.

5. Degkwitz, R.: Convalescent Serum in Measles, Ztschr. f. Kinderh. **25**:134 (May) 1920.

6. Degkwitz, R.: Measles Convalescents' Serum, Ztschr. f. Kinderh. **27**:171, 1920; Serum Prophylaxis in Measles, Deutsche med. Wchnschr. **48**:26 (Jan. 5) 1922; Monatschr. f. Kinderh. **22**:186 (Nov.) 1921.

7. Zingher, A.: Convalescent Whole Blood, Plasma and Serum in Prophylaxis of Measles, J. A. M. A. **82**:1180 (April 12) 1924.

Zingher's publication but were not cited.[4] Estella and de Castro [8] reported good results with dessicated human convalescent serum, and Mery and others [9] had had success with inactivated convalescent serum. Pfaundler,[10] Kroes,[11] Ribeyrolles,[12] Comby,[13] de Jong and Berard,[14] Kutter,[15] Dopter,[16] Blackfan and others,[17] Pesetke,[18] Davis,[19] Torres and Pacheco,[20] and Cambessédès and Joannon [21] had all observed the protective value of convalescent serum. Ruelle [22] obtained protection with convalescent whole blood that was citrated. Savini [23] heated the citrated blood, and Gerlach [24] had conferred immunity with large amounts of defibrinated adult blood, 40 cc. and over. Solomon [25] believed that adult serums were almost as effective as those from convalescing children. Rietschel [26] also found adult whole blood efficacious. Schilling [27] emphasized the point that convalescent serum must be given early in the incubation period to achieve results. He reported protection with blister

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8. Estella, Y. V., and de Castro: Prophylaxis of Measles, J. Arch. españ. de pediat. **6**:517 (Sept.) 1922.

9. Méry, H.; Gastinel, P., and Joannon, P.: Preventive Serotherapy in Measles, Bull. Acad. de méd. de Paris **89**:194 (Feb. 6) 1823.

10. Pfaundler, M.: Prophylaxis in Measles, München. med. Wchnschr. **68**: 277 (March 4) 1921.

11. Kroes, G. M.: Serophylaxis of Measles, Nederl. Tijdschr. v. Geneesk. **2**:1746 (Sept. 14) 1922.

12. Ribeyrolles, A. B.: Prophylaxis of Measles, Semana méd. **2**:546 (Sept. 14) 1922.

13. Comby, J.: Convalescents' Serum in Measles, Arch. de méd. d. enf. **25**:614 (Oct.) 1922.

14. De Jong, S. I., and Berard, E.: Bull. et mém. Soc. méd. d. hôp. de Paris **47**:500 (March 23) 1923.

15. Kutter, P.: Deutsche med. Wchnschr. **47**:1279 (Oct. 20) 1921; Ztschr. f. Kinderh. **36**:119, 1923.

16. Dopter, C.: Convalescents' Serum in Prevention of Measles, Paris méd. **13**:504 (June 2) 1923.

17. Blackfan, K. D.; Peterson, M. F., and Conroy, F. C.: Use of Convalescent Serum as Prophylaxis in Measles and Chickenpox, Ohio State M. J. **19**:97 (Feb.) 1923.

18. Pesetke, S. E.: Serum Prophylaxis in Measles, J. Missouri M. A. **21**:63 (March) 1924.

19. Davis, R. C.: Immunization against Measles with Convalescent Serum, M. Clin. N. Amer. **7**:1259 (Jan.) 1924.

20. Torres, M., and Pacheco, G.: Arch. latino. am. de. pediat. **14**:305, 1920.

21. Cambessédès, H., and Joannon, P.: Médecine **5**:209 (Dec.) 1923.

22. Ruelle, G.: Bruxelles med. **2**:562 (Sept. 15) 1922.

23. Savini, E.: Compt. rend. Soc. de biol. **5**:89, 694, 1923.

24. Gerlach, H.: Prophylaxis of Measles with Adult's Blood, Monatschr. f. Kinderh. **28**:236 (June) 1924.

25. Solomon, G.: Deutsche med. Wchnschr. **49**:1151 (Aug. 31) 1923.

26. Rietschel: Deutsche med. Wchnschr. **49**:1386 (Nov. 2) 1923.

27. Schilling, E.: Klin. Wchnschr. **1**:2471 (Dec. 9) 1922.

fluid (cantharides) from convalescing patients. Maggiore [28] also found that blister fluid would confer immunity. Torday [29] published a review of the literature in 1923, and gave his opinion that if convalescing serum or blood was not obtainable, blood from any older convalescent could be given with good results. The work of di Cristina,[30] Caronia,[31] and others [32] was reviewed by Stefano.[33] The micrococcus described and the results reported with the vaccines produced have not been well accepted (Meyer,[34] Hecht,[35] Takaki [36]) except by a few investigators (Nobel and Schonberger).[37]

Since Zingher's report,[7] the reviews in the literature [38] and the results cited with human convalescing (recent) serum,[39] with convalescent

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28. Maggiore, S.: Serum Prophylaxis of Measles, Pediatria **29**:873 (Oct. 1) 1921.

29. Von Torday, F.: Prophylaxis of Acute Infectious Diseases in Childhood, Jahrb. f. Kinderh. **103**:307 (Dec.) 1923.

30. Di Cristina: Pediatria **22**:721 (1914); **24**:385, 1916.

31. Caronia, G.: Leukolytic Power of Blood Serum, Pediatria **30**:693 (Aug. 1) 1922.

32. Sindoni: Pediatria **31**:145 (July 15) 1923.

33. De Stefano, S.: Present Status of Immunization against Measles, Pediatria **31**:781 (July 15) 1923.

34. Meyer, S.: Is an Immunization against Measles and Production of Measles with Caronia's Cultures Possible? Monatschr. f. Kinderh. **31**:270 (Dec.-Jan.) 1926.

35. Hecht, A. F.: Ztschr. f. Kinderh. **40**:309 (Dec. 16) 1925.

36. Takaki, J.: Cultivation of Virus of Measles and Scarlet Fever According to Caronia, Wien. klin. Wchnschr. **39**:325 (March 18) 1926.

37. Nobel, E., and Schonberger, M.: Prevention of Measles with Caronia's Vaccine, Ztschr. f. Kinderh. **40**:197, 1925.

38. Anderson, J. F.: Modern Methods in Control of Measles, Diphtheria and Scarlet Fever, J. M. Soc. New Jersey **23**:273 (June) 1926. Armstrong, D. B., and Walker, W. F.: Current Immunization Practice in Diphtheria, Scarlet Fever and Measles, Am. J. Pub. Health **16**:1099 (Nov.) 1926. Benson, W. T., and Lawrie, J. D. H.: Sero-prophylaxis of Measles, Edinburgh M. J. **34**:216 (April) 1927. Bischoff, H.: Prevention of Measles, Med. Klin. **22**:1285 (Aug. 20) 1926. Buttenwieser, S.: Prevention of Measles, Deutsche med. Wchnschr. **50**:876 (June 27) 1924. Von Gröer, F., and Redlich, F.: Attempt at Prophylactic Immunization against Measles by Means of Forssman's Antigen, Compt. rend. Soc. de biol. **94**: 354 (Feb. 12) 1926. Jordan, H. P. B.: Measles Immunization, Rhode Island M. J. **9**:71 (May) 1926. Meissner, M.: Prevention of Measles, Med. Klin. **22**: 652 (April 23) 1926. Noeggerath, C.; Oster, H., and Viethen, A.: Critical Estimate of Preventive Measles Serum, Especially of Degkwitz's Serum, from Animals, Klin. Wchnschr. **5**:1186 (June 25) 1926. O'Hara, D.: Recent Progress in Prevention and Treatment of Scarlatina, Measles and Diphtheria, Boston M. & S. J. **195**:561 (Sept. 16) 1926. Richardson, D. L., and Jordan, H. P. B.: Am. J. Pub. Health **17**:607 (June) 1927. Townsend, J. H.: Specific Preventive Measures in Diphtheria, Scarlet Fever and Measles; Review of Our Present Knowledge, Boston M. & S. J. **196**:611 (April 14) 1927. Copeman, W. S. C.: J. Hyg. **24**:427 (Dec.) 1925. Koch, H.: Wien. klin. Wchnschr. **39**:1312 (Nov. 4) 1926. Marie,

(older) serum,[40] with fresh and older whole blood,[41] with blister fluid from convalescing patients,[42] and the reported modifications of measles

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P.: Presse. méd. **30**:456 (May 27) 1922. Seroprophylaxis of Measles, Bull. Acad. de méd. Paris **92**:1495 (Dec. 30) 1924. Gautier, P.: Present Status of Prophylactic Serotherapy of Measles and Whooping Cough, Rev. méd. de la Suisse Rom. **46**:52 (Jan. 25) 1926.

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40. Karelitz, S., and Levin, S. (footnote 39, seventh reference). Debré, R.: Joannon, P.; Bonnet, H., and Cros, J.: Decam. Bull. et mém. Soc. méd. de hôp. de Paris **49**:682 (May 8) 1925. Bivings, L.: South. M. J. **20**:735 (Sept.) 1927. Woeff, S.: Deutsche med. Wchnschr. **50**:1545 (Nov. 7) 1924.

41. Adler, S. W.: Attempted Prevention of Measles in Private Practice, Minnesota Med. **7**:600 (Sept.) 1924. Brügger (footnote 39, second reference).

with graduated doses of convalescing (recent) serum or whole blood have [43] well established the original observations that the blood of persons convalescing from measles contains a protective antibody which, if given in large enough amounts early enough in the incubation period, will usually protect the exposed person against measles. Five cubic centimeters for children 5 years of age and 10 cc. for older patients, of human blood serum or plasma, obtained within eight to ten days after defervescence, or within ten to twelve days after the initial appearance of the rash, injected intramuscularly not later than the fourth day of the incubation period, will usually confer a passive immunity of from six to ten weeks' duration. From 15 to 30 cc. of whole blood obtained and injected under the same conditions will be found as effective. The protective power decreases after recovery from the disease. Pooled blood, serum or plasma is preferable and a preservative is added if the material is to be kept (phenol, tricresol or quinosol). The preserved serums or plasmas will probably retain their potency for from three to six months if kept at about 5°C.

However effective human convalescent blood or serum, its use is limited. Adult donors are scarce and children recovering from measles cannot well spare blood. Also, the passive immunity [44] conferred is of comparatively short duration. Herrman's method of active immunization, while probably effective, also offers practical limitations. The method of Debré and others [45] for active immunization required blood taken at the onset of the eruption. The duration of the immunity has not been determined. Further Italian reports concerning the etiologic

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Gerlach, H.: Prophylaxis of Measles with Adult's Blood, Monatschr. f. Kinderh. **28**:236 (June) 1924. Haas, S. V., and Blum, J.: The Prophylactic Value of Blood of Convalescents in Measles, J. A. M. A. **87**:558 (Aug. 21) 1926. Hilsinger, W.: Blood from Adults for Prophylaxis Against Measles, Arch. f. Kinderh. **76**: 211 (Aug.) 1925. Karelitz, S., and Levin, S. (footnote 39, seventh reference). Ockel, G.: Med. Klin. **22**:886 (June 4) 1926. Townsend, J. H. (footnote 39, twenty-fourth reference). Buttorff, G. S.: Kentucky M. J. **25**:406 (Aug.) 1927. Forbes, R. P., and Green, B.: Modified Measles, J. A. M. A. **89**:1601 (Nov. 5) 1927. Bivings, L. (footnote 40, third reference).

42. Modinos, P.: Blister Fluid for Serum-Prophylaxis Against Measles, Bull. et mém. Soc. méd. d. hôp. de Paris **50**:404 (March 12) 1926; Medicine **8**:201 (Dec.) 1926.

43. Moro, E., and Müller, E.: Atypical Measles in Children with Incomplete Protection from Convalescents' Serum, Jahrb. f. Kinderh. **109**:127 (July) 1925. Moro, E.: Klin. Wchnschr. **4**:1719 (Sept. 3) 1925. Degkwitz, R.: Measles Convalescent's Serum, Monatschr. f. Kinderh. **22**:186 (Nov.) 1921. Park, W. H., and Freeman, R. G., Jr. (footnote 39, sixteenth reference).

44. Herrman, C.: Immunization Against Measles, Arch. Pediat. **32**:503 (July) 1915; **39**:607 (Sept.) 1922.

45. Debre, R., and Papp, K.: Disappearance of Positive Skin Reactions to Tuberculin During Measles, Ann. de méd. **19**:576 (June) 1926.

organism [46] and vaccines prepared [47] are not convincing. The reported results with normal horse serum [48] are doubtful as are the results reported with Forrsman's antigen.[49] Until the detoxified toxins [50] and anatoxins [51] are made available for measles, animal immune serums offer the most favorable solution of the problem of prevention.

In January, 1926, Degkwitz [52] reported the results obtained in the prevention of measles with a specific serum obtained from animals. Sheep and monkeys were repeatedly infected with filtrates from the nasopharyngeal secretion of patients with measles or with tissue cultures inoculated with the virus. One hundred and twenty-two of 134 children were protected when the serum was injected between the seventh and eleventh day. Later in the year Degkwitz reported further results of his antiserum.[53] A new, secret preparation of serum was made available commercially which created considerable criticism.[54] Some of the results reported with Degkwitz's animal serum were favorable,[55] but the majority of authors criticized Degkwitz severely, particularly for his procedure in the commercialization of the antiserum.[54] The unfavorable results cited not only mak failure to protect against the disease but an attenuation

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46. Caronia, G.: Specific Prevention of Scarlet Fever and Measles, Arch. españ. de pediat. **10**:449 (Aug.) 1926; Policlinico **32**:1357 (Sept. 28) 1925. Guardabassi, M.: Il virus morbilloso, Pediatria **35**:801 (Aug. 1) 1927.

47. Annechino, F. P.: Vaccine Prevention of Measles, Pediatria **33**: 1006 (Sept. 15) 1925. Emmanuele, A.: Results of Prevention of Measles with Caronia's Vaccine in Infant's Asylum, Pediatria **34**:30 (Jan. 1) 1926. Ricciardi, L.: Pediatria **33**:1333 (Dec. 15) 1925.

48. Pontano, T., and Alba, C.: Ann. d'ig. **37**:515 (Aug.) 1927.

49. De Gröer, F., and Redlich, F. (footnote 38, sixth reference).

50. Larson, W. P.; Huenekens, E. J., and Colby, W.: Immunization Against Scarlet Fever, J. A. M. A. **86**:1000 (April 3) 1926. Larson, W. P., and Eder, H.: Immunization Against Diphtheria with Toxin Detoxified with Sodium Ricinoleate, ibid. **86**:998 (April 3) 1926.

51. Ramon, G.: Compt. rend. Acad. d. sc. **177**:1338, 1923.

52. Degkwitz, R.: Specific Serum Obtained from Animals for Prevention of Measles, München. med. Wchnschr. **73**:181 (Jan. 29) 1926.

53. Degkwitz, R.: Measles Serum Obtained from Animals, Klin. Wchnschr. **5**:1361 (July 23) 1926.

54. Kaupe, W.: Degkwitz's Measles Serum, Med. Klin. **22**:213 (Feb. 5) 1926; **22**:455 (March 19) 1926. Nocht, B.: Specific Serum Obtained from Animals for Prevention of Measles; Comment on Degkwitz's Article, München. med. Wchnschr. **73**:366 (Feb. 26) 1926. Rudder, B.: Experiences with New Measles Serum from Animals, Klin. Wchnschr. **5**:1406 (July 30) 1926. Schlossman, A.: Measles Serum from Animals: Comment on Degkwitz's Article, Klin. Wchnschr. **5**:1824 (Sept. 24) 1926; Deutsche med. Wchnschr. **52**:1241 (July 23) 1926. Degkwitz, R.: Degwitz's Serum, Comment on Kaupe's Article, Med. Klin. **22**:454 (March 19) 1926; Deutsche med. Wchnschr. **52**:1419 (Aug. 20) 1926.

55. Anderson, M. S.: Ugesk. f. Laeger **80**:1190 (Dec. 30) 1926. Degkwitz, R.: Klin. Wchnschr. **5**:2407 (Dec. 17) 1926. Wiese, O.: Experiences with Degkwitz's Measles Antiserum, München. med. Wchnschr. **73**:184 (Jan. 29) 1926.

of the disease with death in some cases.[56] The effectiveness of the serum probably depends entirely on the method of preparation.[57]

Also, in January, 1926, and shortly antedating Degkwitz, Tunnicliff and Hoyne[58] reported the production of an antimeasles diplococcus serum in goats.

> The immune goat serum was prepared by the intravenous injection of first killed, later living cultures and filtrates of green producing diplococci isolated from the blood, nose, throat and sputum of patients with measles. After one year of such immunization, the Zinsser-Grinnell blood clot method of immunization was used. The immune goat serum was not concentrated.

Tunnicliff[59] and Tunnicliff and Taylor[60] later reported observations on an extracellular as well as an intracellular toxin produced by the specific diplococcus of measles which gave a positive skin reaction in persons who had not had measles but not in those with a positive history of the disease. This toxin was neutralized by convalescent human serum and by the serum of goats immunized with measles diplococci, but not by normal goat serum. These observations and others[61] seem to establish the diplococcus described by Tunnicliff[62] as the etiologic agent of

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56. Baron, C.: Med. Klin. **23**:48 (Jan. 14) 1927. Erickson, J.: Ibid. **22**:1332 (Aug. 27) 1926. Glaser, F.: Ibid. **22**:766 (May 14) 1926. Hagen, W.: Deutsche med. Wchnschr. **52**:871 (May 21) 1926. Kochmann, R.: Practical Experiences with Degkwitz's Measles Serum, ibid. **52**:565 (April 2) 1926. Mosse, K.: Klin. Wchnschr. **5**:708 (April 16) 1926. Progulski, S., and Redlich, F.: Degkwitz's New Measles Serum, ibid. **5**:146 (Aug. 6) 1926. Reuter A.: Short Report on Degkwitz's Measles Serum, Med. Klin. **22**:1181 (July 30) 1926. Zoepffel, H.: München. med. Wchnschr. **74**:150 (Jan. 28) 1927.

57. Rudder, B. (footnote 54, third reference). Anderson, M. S. (footnote 55, first reference). Degkwitz, R. (footnote 55, second reference). Weise, O. (footnote 55, third reference).

58. Tunnicliff, R., and Hoyne, A. L.: Further Studies on Diplococcus from Measles; Prevention of Measles by Immune Goat Serum, J. Infect. Dis. **38**:48 (Jan.) 1926. Personal communication from the author.

59. Tunnicliff, R.: Further Studies on Diplococcus in Measles, Measles Skin Reaction, J. Infect. Dis. **37**:193 (Sept.) 1925.

60. Tunnicliff, R., and Taylor, R. E.: Skin Tests in Measles, J. A. M. A. **87**:846 (Sept. 11) 1926.

61. Duval, C. W., and Hibbard, R. J.: Further Studies upon the Etiology of Measles, Proc. Soc. Exper. Biol. & Med. **24**:519 (March) 1927. Cary, W. E., and Day, L. A.: Etiology of Measles, J. A. M. A. **89**:1206 (Oct. 8) 1927.

62. Tunnicliff, R.: The Cultivation of a Micrococcus from Blood in Pre-Eruptive and Eruptive Stages of Measles, J. A. M. A. **68**:1028 (April 7) 1917; Immune Reactions of Measles, J. Infect. Dis. **22**:462, 1918; Observations on Throat Smears in Measles, Rubella and Scarlet Fever, J. A. M. A. **71**:104 (July 13) 1918. Tunnicliff, R., and Brown, M. W.: J. Infect. Dis. **23**:572 (Dec.) 1918. Tunnicliff, R.: Agglutination in Measles, J. Infect. Dis. **24**:78 (Jan.) 1919; Bacterium in Sputum in Measles, ibid. **24**:181 (Feb.) 1919. Tunnicliff, R., and Moodie, W. B.: Experimental Measles by Inoculation of Monkeys, Guinea-Pigs and Rabbits with Green Producing Streptococcus, ibid. **31**:382 (Oct.) 1922.

measles. The organism described by Ferry [63] is similar to that of Tunnicliff.

Hoyne and Gasul [64] first reported the clinical results of Tunnicliff's antimeasles goat serum. Thirty-nine children with definite exposure to measles were given the serum and thirty-four of these did not develop the disease. In December, 1926, Tunnicliff and Hoyne [65] reported further clinical results with the goat serum in 105 persons; 97 per cent of those who received the serum in the first four days after exposure did not develop measles. In 1927, Tunnicliff and White [66] described the production of a specific immune measles serum with Tunnicliff's organism in a horse.

In April, 1926, a case of measles developed in the infants' ward of the Milwaukee Children's Hospital. Through the courtesy of Dr. Ruth Tunnicliff antimeasles goat serum was made immediately available. The

TABLE 1.—*Measles Antidiplococcus Serum (Conc.) (Horse) (E. R. Squibb and Sons)*

Patient	Age in Years	Dose of Serum, Cc.	Day After Exposure	Result	Serum Reaction
J. G.	3½	5	4th	No measles	None
D. B.	2½	5	4th	No measles	None
S. R.	11	5	4th	No measles	None
E. T.	9	5	4th	No measles	None
V. S.	11	5	4th	No measles	None
R. R.	3½	5	4th	No measles	None
J. K.	7	5	4th	No measles	None
O. H.	6	5	4th	No measles	Slight

majority of the infants who received injections of 5 cc. or more of the goat serum, on or before the fourth day of incubation, did not develop measles. Serum injected after the fifth day of incubation did not prevent the disease and when injected on the fifth day it was occasionally successful. Doses of from 2 to 4 cc. injected before the fifth day of incubation were followed by a mild fever for two to three days and a transient rash. Several infants who received from 2 to 4 cc. of serum before the fifth day of incubation developed mild cases of measles

63. Ferry, N. S.: Etiology of Measles, Am. J. Pub. Health **17**:565 (June) 1927. Ferry, N. S., and Fisher, L.: Measles Toxin, J. A. M. A. **86**:932 (March 27) 1926.

64. Hoyne, A. L., and Gasul, B. M.: Measles Prophylaxis, Immune Goat Serum, J. A. M. A. **87**:1185 (Oct. 9) 1926.

65. Tunnicliff, R., and Hoyne, A. L.: Prevention of Measles by Immune Goat Serum, J. A. M. A. **87**:2139 (Dec. 25) 1926.

66. Tunnicliff, R., and White, B.: Anti-Measles Diplococcus Serum: Preliminary Communication, Boston M. & S. J. **197**:272 (Aug. 18) 1927.

from twenty-one to thirty days after exposure. All infants over four months of age who were exposed developed the disease. These cases are included in the report of Tunnicliff and Hoyne.[65]

A case of measles developed again in June, 1927. Antimeasles diplococcus, goat and horse serum (E. R. Squibb and Sons) were supplied

TABLE 2.—*Measles Antidiplococcus Serum (Goat)*

Patient	Age	Dose of Serum, Cc.	Day After Exposure	Result	Serum Reaction
H. S.	5 mo.	7	5th	No measles	None
W. D.	4 mo.	7	1st	No measles	None
E. H.	2½ wk.	5	1st	No measles	None
T. S.	4 mo.	5	4th	No measles	None
J. S.	20 mo.	7	5th	No measles	None
B. C.	23 mo.	7	5th	No measles	None
E. P.	5½ mo.	7.5	4th	No measles	None
D. D.	5 mo.	7.5	4th	No measles	None
O. B.	3 yr.	7.5	4th	No measles	None
R. K.	5 yr.	7.5	4th	No measles	None
G. C.	5 yr.	7.5	4th	No measles	None
R. J.	2 yr.	5	4th	No measles	None
D. R.	8½ mo.	5	4th	No measles	None
K. O.	8 mo.	2	4th	No measles	None
G. C.	15 mo.	10	2nd	No measles	None
D. C.	1 yr.	10	5th	No measles	None
J. A.	10 mo.	5	5th	No measles	None
H. N.	11 mo.	5	5th	No measles	Emesis slight erythema 15 minutes after injection
M. K.	18 mo.	5	5th	No measles	None
V. D.	23 mo.	5	5th	No measles	Mild on 6th day
E. C.	16 mo.	5	5th	No measles	None
B. B.	7½ mo.	2½	2nd	No measles	None
A. H.	6 mo.	2½	2nd	No measles	None

TABLE 3.—*Measles Antidiplococcus Serum (Goat)*

Patient	Age	Dose of Serum Cc.	Day After Exposure	Day of Eruption	Measles †			Complications
					Days of Duration Fever	Maximum Temperature	Koplik's	
J. P.	4½ mo.	5	2nd	20	3	103	Yes	None
G. R.	9 mo.	7	3rd	16	4	103	Yes	None
D. T.	5 mo.	7	5th*	2	14	102	Yes	Lobar pneumonia
J. C.	3 yr.	7½	4th	14	4	103	Yes	None

* Exposure may have occurred before admission to the hospital.
† After injection of serum.

through the courtesy of Dr. Tunnicliff. Thirty-five exposed infants and children with no history of previous measles were given antimeasles diplococcus serum. Eight children received concentrated horse serum, and none developed the disease (table 1). Twenty-seven infants and children were given goat serum, twenty-three did not develop the disease (table 2), while three had mild cases of measles, eighteen, nineteen and twenty-two days after exposure (table 3). One infant received

the injection supposedly on the fifth day after exposure and measles developed on the second day following (table 3). In this case, the serum was given too late for protection or modification of the disease. Two exposed infants, aged 9 and 11 months, who were not given serum developed measles.

Excluding the infant who received the serum two days before developing the disease, there was complete protection from measles in thirty-one of thirty-four patients inoculated. There was a modification of the disease in the remaining three.

167 Seventeenth Street.

Pediatric Biographies

JONAS AND RAYNALDE*

JOHN RUHRÄH, M.D.
BALTIMORE

The work of Metlinger was destined to be widely read owing to rather fortuitous circumstances. It was a popular book and was reprinted many times; early in the sixteenth century it had its fortune linked with more than one other book, but chiefly with the work on obstetrics by Eucharius Röslin, or Rhodion, as he is sometimes called. This work, generally known as "De Partu Hominis," appeared in 1513 at Frankfort-am-Main with the title of "Der Swangern Frawen und Hebammen Rosegarten." In those days and often since, it has been called the "Rosegarten." It was largely made up of the work of the early masters and had a great vogue, not only in the original German, but in Latin, French, Dutch and English. Some of these editions included a more or less altered text of Metlinger's book on children, sometimes giving him credit and sometimes using the text anonymously.

In 1840, there appeared in London an English translation of Röslin's work, evidently from the French edition of 1538, and this included the book on children. This book is rare, but it may be seen without the plates in the British Museum, and the Library of the College of Physicians in London boasts two complete copies. Of this book, Dibdin wrote the following in his edition of Ames' "Antiquities":

> *The Byrth of Mankynde.* 1540. Quarto. The byrth of mankynde newly translated out of Laten into Englysshe. In the which is entreated of all suche thynges the which chaunce to women in theyr labor, and all suche infyrmitees whiche happen unto the Infantes after they be delyuered. And also at the latter ende or in the thyrde or last boke is entreated of the conception of mankynde, and howe manye wayes it may be letted or furtheryd, with diuers other fruytefull thynges, as doth appere in the table before the booke. *Cum priv. regal. ad impr. sol.*

On the back of the title page is a sort of religious "admonicion to the reader," which is followed by a dedication of six pages "Unto the most gracious and in all goodnesse most excellent vertuous Lady Quene Katheryne wyfe and most derely belouyd spouse unto the most myghty sapient Christen prynce Kynge henry the VIII. *Richard Ionas* wyssheth perpetuall ioye and felicyte."

In passing it may be mentioned that one of the best accounts of the book is by J. W. Ballantyne, published in *The Journal of Obstetrics and Gynaecology of the British Empire* in 1906, 1907 and 1910.

* Received for publication, May 17, 1928.

¶ Item take the iuyce of centinodium and the whyte of an egge: and temper them toge ther/to the whiche adde the pouder of dryed red roses / the pouder of hematites / maſtyke/frankencenſe/ bole armenyacke / ſanguis draconis and plida: of all theſe myxed to ge: ther make a plaſter / and laye it to the infan: tes bellye.

¶ Item to waſſhe the chylde with the wa ter in the which be ſoden leues of red rooſes is very good. Item take the iuyce of conſery and the iuyce of plantayne the moze and the leſſe/and in this put claye of an olde furnyſe oz ouen/and make of it a plaſter / and laye it to the chyldes bellye.

¶ To vnlooſe the chylde beynge bounden.

Yf the chylde be ſo bounde / that it can not ſege: then make a ſuppoſitary of hony ſoden tyll it be harde and maſſye/and let the ſuppo ſitary be of the length of your lyttell fynger/ & the byggencſſe of two whyteſtrays bounde to gether/then dyppe it into oyle and conuey it into the chyldes foundament.

¶ Item lykewyſe ye maye make a ſuppoſi tary of the ſtalke and rote of betes / oz els of the rote called ozeſſe oz flowze de luce rote/ made of the quantite befoze ſpoken of/ & con: neyed into the ſyttynge place of the chylde.

¶ Item to geue to the infant as much ho: ny as a peaze to dzynke & to rubbe the bellye a lyttell/and to ſople it with a pece of wooll dypped in oyle / oz dypped in bulles galle / & layde to the nauell. Item ye maye geue vnto the nource a medycyne whiche hathe vertue to vnbynde and looſe/and the next day after let the chylde ſucke her / and it wyll looſe al: ſo the chylde.

¶ Item take of mouſe dounge half a dzam and temper it with the fatte in the kydnees of a goote / & make a ſuppoſitoz of the ſame. Item take of ſmall mallowes/of greate mal lowes of eche an handefull of fenegreke and lynſede of eche an handefull/of holyoke two ounces/ of fygges the nombez of. x. ſethe all theſe together in water/ & then ſtampe them in a mozter/and put vnto it of butter and of hennes grece. ij. ounces / and of ſafrane one ſcruple / and make a plaſter of it vppon a lynnen clothe of the thyckeneſſe of a ſtralbe/ and laye it to the chyldes bellye a daye and a nyghte.

This translation was by Richard Jonas, about whom nothing is known except that he is described as "a certayne studious and diligent Clarke" in the prologue of some of the augmented editions which were subsequently published by Thomas Raynalde.

Raynalde says:

> Wherefore not to come to our purpose, ye shal understand that about a thre or foure yeres past, a certayne studious and diligent clarke, at the request and desyre of diuers honest and sad matrones, beynge of hys acquayntaunce, dyd translate out of Latin into English a great part of thys boke, entiteling it according to the Latine inscription (de partu hominis, that is to saye: of the byrth of mankynd) which we nowe do name (The womans boke) (for so moch as the most parte or well neare all therein entreated of, doth concerne and touche onely women).

Little is known of Thomas Raynalde, except that he was a physician and had traveled abroad to Venice and Padua and Paris. While in Venice, he had a book printed about the virtues of a remedy which he called "oil imperial." There was a printer of the same name in London between 1541 and 1545, but there is some doubt as to whether it was the physician or another man.

In 1545, Raynalde "corrected and augmented" the book so that it was almost a new work. For over a hundred years it had a wonderful vogue, and it was reprinted about a dozen times; the last imprint bears the date 1676. Some changes were made from time to time and some additions.

The text of Metlinger had passed through so many hands and had been so added to and rewritten that in Jonas' translation it seems like another book. It furnished some of the material for Phaer's, "Boke of Children," but not much. Some idea may be had of the style by the following quotation:

OF GOOGLE EYES OR LOKYNGE A SQUYNT

> If the chylde have google eyes or that it loke a squynt then fyrst set the cradel in such a place that the lyght maye come directelye and ryght in the chyldes face neyther in the one syde neyther in the other, neyther above the heade, leste it torne the syghte after the lyght. Also marke on whiche syde that the eyes do gogle, and let the lyghte come unto it on the cotrary syde, so to retorne the syght. And in the nyght season set a candell on the contrarye syde, so that by this meane the goglynge of the eyes may be retorned to the ryghte place. And farther it shall be good to hange clothes of divers and freshe coloures on the contrary syde and especially of the coloure of lyght grene or yelowe, for the chylde shall have pleasure to beholds these strange coloures and in retornynge the eye syghte towarde suche thynges it shal be occasion to rectifye the syght agayne: and this shall be sufficient for this tyme of the dyseases of chyldren, after they be borne makynge here an ende of this seconde boke.

News and Comment

DEATH OF DR. BALDWIN

Bird T. Baldwin, Ph.D., since 1917 director of the Iowa Child Welfare Research Station and research professor in educational psychology at the State University of Iowa, Iowa City, died, May 12, after a few days' illness due to erysipelas. Dr. Baldwin was widely known for research in child welfare work; he had taught at several universities, and was the author of articles, bulletins and reviews on psychologic subjects.

DEDICATION OF NEW WING IN CHILDREN'S HOSPITAL IN SEATTLE

The Children's Orthopedic Hospital, Seattle, recently dedicated a new four-story wing. There is a swimming pool where children crippled by infantile paralysis may exercise.

DECISION ON SHEPPARD-TOWNER ACT

Federal financial assistance under the provisions of the Sheppard-Towner Act will cease, June 30, 1929, and states having an unexpended balance of federal funds on that date must return such balance to the United States Treasury. This ruling was recently made by U. S. Controller-General McCarl in response to a request from the state of Georgia for permission to use unexpended federal funds after the repeal date of the Sheppard-Towner Act. The effect of this decision will be to shut off on June 30, 1929, all federal money for this work, both at Washington and throughout the country.

BEQUESTS AND DONATIONS

By the will of the late Miss Martha T. Smith, the Babies' Hospital of New York receives $10,000.

By the will of the late George T. Roberts, the Children's Hospital, the Philadelphia Orthopedic Hospital and the House of St. Michael and All Angels for Crippled Children of Philadelphia receive about $60,000 each.

By the will of the late Edward B. Butler, the Children's Memorial Hospital of Chicago receives $10,000, and the Walter Scott Industrial School for Crippled Children of New York receives $5,000.

The will of Thomas Alexander Forsyth, filed, April 1, in Boston bequeaths $2,000 to each of the following institutions: Children's Hospital, Home for Aged Men, Home for Aged Women, Home for Aged Couples, Holy Ghost Hospital and St. Luke's Home for Convalescents, and all of the residue of the estate after various other bequests to the Forsyth Dental Infirmary for Children—all of Boston and Cambridge, Mass.

By the will of Judge Wesley H. Richards, the Children's Hospital of Cincinnati receives $10,000.

DEATH OF FERNANDES FIGUEIRA

The well known Brazilian pediatrician, Fernandes Figueira, died recently at Rio de Janiero at the age of 70.

PROMOTIONS AT CALIFORNIA MEDICAL SCHOOL

The University of California Medical School announces the promotions of Dr. Olga L. Bridgman to professor of pediatrics and psychology, and Dr. Florence M. Holsclaw to associate clinical professor of pediatrics.

NEW MEMBERS OF AMERICAN PEDIATRIC SOCIETY

At the recent meeting of the American Pediatric Society there were elected to honorary membership Prof. Adalbert Czerny of Berlin and Prof. G. Araoz Alfaro of Buenos Aires.

The following were elected to active membership:

Charles Anderson Aldrich, 545 Lincoln Ave., Winnetka, Illinois.

Ethel Collins Dunham, 211 St. Ronan St., New Haven, Conn.

Irvine McQuarrie, Strong Memorial Hospital, University of Rochester, Rochester, N. Y.

William A. Mulherin, 753 Broad St., Augusta, Ga.

Thomas Milton Rivers, Rockefeller Institute for Medical Research, New York.

James Buren Sidbury, 15 North 5th St., Wilmington, N. C.

NEW UNIT OF SLOANE'S HOSPITAL FOR WOMEN

On June 4, 1928, the sixth hospital unit began to operate at the Medical Center at One Hundred Sixty-Eighth Street and Broadway, New York, when the Sloane Hospital for Women opened its doors for the reception of private patients. Sloane Hospital will continue its cooperation with the College of Physicians and Surgeons and the Vanderbilt Clinic.

Abstracts from Current Literature

Anatomy and Physiology

THE ANTAGONISTIC ACTION OF CARBOHYDRATES AND ELECTROLYTES ON THE BEHAVIOR OF THE LEUKOCYTES AND THE EXCRETION OF ARSENIC FOLLOWING THE ADMINISTRATION OF THE ARSPHENAMINES. C. N. MYERS and E. F. MUELLER, Am. J. Syph. **12**:157 (April) 1928.

Previous investigations have shown that a peripheral leukopenia develops with the intravenous injections of arsphenamine, the neutrophils being decreased as a result of increased activity of the autonomic nervous system. This reaction is not noted with silver arsphenamine.

The nitritoid crisis, the clinical observations and the chemical determinations for arsenic show that functional disturbance precedes the increased arsenic in the tissue involved. It may be assumed that a state of chronic irritation follows the acute derangement of the vasomotor system. This is not in direct proportion to the amount of arsenic retained by the tissue, but is somewhat dependent on individual susceptibility. This continued irritation is illustrated by the development of clinical symptoms several days or weeks after the administration of the arsenic.

The authors show that carbohydrates, i. e., 2.5 per cent lactose or the electrolytes, 0.4 per cent sodium chloride solution, will prevent the symptoms of shock and the peripheral leukopenia, while it greatly increases the rate of excretion of the arsenical. The authors raise the question as to the danger of decreasing the therapeutic efficiency by increasing the excretion in this manner.

The white blood cells which migrate from the periphery are the fully developed neutrophils. The rate of migration of the leukocytes is a measure of the response of the autonomic nervous system to the arsenical.

McBRIDE, Sioux City, Iowa.

CONGENITAL ABNORMALITIES OF THE URINARY TRACT IN CHILDHOOD. HENRY F. HELMHOLZ, J. A. M. A. **89**:1932 (Dec. 3) 1927.

Congenital abnormalities of the urinary tract are more common than is ordinarily believed. Careful history taking, careful examination of the areas of the kidney and bladder, and the assumption that chronic pyelitis that cannot be cured shortly by intensive treatment warrants complete urologic examination, will lead to detection of such anomalies. Of the ninety-four cases analyzed, there were eighteen anomalies of the kidney, fourteen of which were hydronephrosis; thirteen urethral anomalies (nine dilated ureter); six urethral anomalies and fifty-seven anomalies of the bladder — thirty-four exstrophy; twenty-two of neuromuscular dysfunction and one diverticulum. Methenamine with sufficient ammonium chloride to render the urine acid to a hydrogen concentration of from 5.5 to 5.0 is the most useful urinary antiseptic. If marked urinary frequency and urgency or hematuria indicate overstepping of the tolerance for the drug, it is discontinued, water is forced and sodium bicarbonate given.

BONAR, Salt Lake City.

Pathology, Bacteriology and Biochemistry

LOCAL AND SYSTEMIC CHANGES INDUCED BY LIPOID SOLVENTS IN ANIMALS FED ON DIETS VARYING IN VITAMIN CONTENT. LOUIS H. JORSTAD and CHARLES G. JOHNSTON, Am. J. Path. **3**:489, 1927.

Various oils and fats act like coal tar when injected into subcutaneous tissue of animals. All of them dissolve the lipoids of the cell and may be classed as lipoid solvents. The cellular activity about droplets of various

lipoid solvents injected into the subcutaneous tissue of rats is greatly increased by feeding a diet rich in vitamin A. The lipoid solvent remains en masse in an animal fed a ration deficient in vitamin A and disperses into smaller droplets in the animal fed a ration rich in vitamin A. The tissue reaction about the lipoid solvent is altered in degree if the fats are removed from the solvent with ether before it is injected into the tissue. Rats injected subcutaneously with certain lipoid solvents or mixtures of them and fed a diet rich in vitamin A suffer a massive fatty infiltration of the liver. This infiltration occurs at different periods of time after the injection of the different lipoid solvents. Chloroform produces a necrosis of the liver because it diffuses rapidly throughout the system. This lesion is similar to that produced locally by coal tar in the tissue.

AUTHORS' SUMMARY.

THE RED-CELL SEDIMENTATION TEST IN CHILDREN. E. M. GREISHEIMER, J. A. MYERS, N. P. PETERSON, A. D. KLEIN and A. COLLINS, Am. Rev. Tuberc. **16**:344, 1927.

No correlation was found between age and the sedimentation index. The latter seems higher in children than in adults. No marked differences were found between girls and boys. Weight did not seem to be a determining factor in the sedimentation test. There were few children who showed a positive Larson ring test, but these few showed a faster sedimentation than the children having negative tests. The boys having positive Pirquet or Mantoux tests showed a faster sedimentation rate than those having negative tests, but the condition was reversed in the girls. No definite relationship between the percentage of hemoglobin and the sedimentation index or twenty-four hour reading was found. The latter did not appear to be related to the red cell count. The relation between leukocyte count and sedimentation rate was variable.

H. J. CORPER.

THE MALTASE OF THE DIPHTHERIA BACILLUS. JOHN Y. SUGG, WILLIAM L. FLEMING and JAMES M. NEILL, J. Exper. Med. **46**:909, 1927.

Diphtheria bacilli possess a heat-labile, endocellular maltase, which retains its activity in sterile solutions of the intracellular substances which are liberated by physical disintegration of the bacterial cells. The proof of the maltase activity and the detection of the hexose products constitute experimental evidence that the living diphtheria bacillus attacks maltose by way of a preliminary hydrolysis.

CORYNEBACTERIUM ULCERANS: A PATHOGENIC MICRO-ORGANISM RESEMBLING C. DIPHTHERIAE. RUTH GILBERT and F. CONSTANCE STEWART, J. Lab. & Clin. Med. **12**:756, 1927.

The micro-organisms described differ from true diphtheria bacilli in the following respects: rapid change in morphology from bacillary to coccoid forms, usually in twenty-four hours; liquefaction of gelatin; nonreduction of nitrates; reaction from intracutaneous injection of micro-organisms on both normal guinea-pigs and on those immunized with diphtheria antitoxin; formation of extensive ulcers on animals inoculated subcutaneously with a living culture, and production of a soluble toxin for which a neutralizing antitoxin was prepared. The serum of the horse thus immunized showed a definite but limited increase in its content of diphtheria antitoxin. Although *Corynebacterium ulcerans* differs from the true diphtheria bacillus in these respects, it is doubtless a closely related species. From the evidence of pathogenicity that the cultures manifest, it seems probable that it may be of etiologic significance in some of the inflammatory or ulcerative lesions, especially those of the nose and throat.

RÔLE OF THE SKIN IN THE PRODUCTION OF ANTIBODIES, ANAPHYLAXIS AND ANTI-ANAPHYLAXIS. E. KLUKHINE, Ann. de l'Inst. Pasteur **41**:1108, 1927.

Following the cutaneous application of certain antigens, antibodies are elaborated in the serum only when the epidermis presents marked alterations; guinea-pigs may thus be sensitized to horse serum. With animals sensitized parenterally to horse serum, a true anaphylactic shock is not produced when the following injection is made subcutaneously. Sensitized guinea-pigs take an antianaphylactic vaccination by the procedure of Besredka, i. e., simple application of the serum to the scarified skin.

AUTHOR'S SUMMARY.

PHYSICOCHEMICAL NATURE OF DIPHTHERIA TOXIN AND ANATOXIN. V. KOULIKOFF and P. SMIRNOFF, Ann. de l'Inst. Pasteur **41**:1166, 1927.

Acid precipitation of toxin gave precipitates having minimum lethal doses of 0.0000006 to 0.00000028 Gm.; anatoxin thus precipitated was capable of immunizing in a dose of 0.00005 Gm. The toxicity of a solution of precipitate rapidly disappears even at 5 C. and a new precipitate forms. This neutralization of toxin and formation of a second precipitate is discussed.

M. S. MARSHALL.

THE TISSUE REACTION EFFECT OF BACTERIA: III. THE EFFECT OF STREPTOCOCCI, ESPECIALLY THE SCARLET FEVER STREPTOCOCCI. H. DOLD, Centralbl. f. Bakteriol. **102**:417, 1927.

Dold tested 160 strains of streptococci by the method of intracutaneous injection into rabbits, previously described by him. He divides them according to their effects, into three types, viz; type I, streptococci which cause only a slight erythema with only a slight infiltration; type II, streptococci which lead to a strong infiltration with deep inflammation and necrosis, but remains localized and heals in from one to three weeks, and type III, with a rapidly developing and spreading inflammation and leading to death of the rabbit within a few days. Forty strains from cases of scarlet fever belonged to types I and II.

THE VALUATION OF THE ANTIGENIC PROPERTIES OF THE DERIVATIVES OF DIPHTHERIA TOXIN BY MEANS OF THE RING PRECIPITATION METHOD. E. HOEN, L. TSCHERTKOW and W. ZIPP, Ztschr. f. Immunitätsforsch. u. exper. Therap. **53**:20, 1927.

The authors describe experiments as to the antigenic nature and properties of diphtheria toxin and anatoxin as influenced by heat and H-ion concentration. They find, in the case of diphtheria toxin, that heating leads to a proportionate loss of both antigenic and precipitating properties, whereas the antigenic properties of anatoxin are not so seriously impaired by heating until a temperature of from 60 to 65 degrees is reached. A p_H of from 8.4 to 6 does not influence the precipitation reactions of diphtheria toxin by the ring method. The authors feel that their method is superior to Ramon's flocculation method.

PAUL R. CANNON.

Nutrition

A RACHITIC-LIKE DISTURBANCE IN EXTREME HYPOTHYROIDISM. M. M. KUNDE and A. J. CARLSON, Am. J. Physiol. **82**:630, 1927.

In young rabbits, thyroidectomized between two and three weeks after birth, a disturbance in skeletal development was found, showing a fundamental resemblance to that of clinical rickets, accompanied by severe anemia. Control litter mates showed that this condition was not due to dietary deficiency. Blood calcium was normal or only slightly below normal, and acid-soluble phosphorus in the serum was low.

THE INFLUENCE OF THE THYROID GLAND ON THE PRODUCTION AND CONTROL OF EXPERIMENTAL RICKETS. M. M. KUNDE and L. A. WILLIAMS, Am. J. Physiol. **83**:245, 1927.

In cretin rats the addition of cod liver oil to a rickets-producing diet, and to a diet nutritious and rich in vitamins, was without effect in both instances in preventing the development of that disease, as indicated by histologic changes in the epiphyses.

H. E. EGGERS.

DEFICIENCY IN VITAMIN A AND METAPLASIA. HARRY GOLDBLATT and MARIA BENISCHEK, J. Exper. Med. **46**:699, 1927.

A dietary deficiency of vitamin A alone is adequate to induce metaplasia of columnar, cuboidal and transitional epithelia to the squamous, keratinizing type in some organs. Epithelial metaplasia to the squamous keratinizing type is of such frequency in young rats kept on a diet deficient in vitamin A for a long period of time (ten weeks or longer) as to constitute a good morphologic indicator of the deficiency of this vitamin in the diet. The metaplastic changes are as frequent and as great in rats on a diet deficient in vitamin A alone as in those on a diet deficient in vitamins A and D. Inadequate food, provided the vitamins are supplied, does not induce the metaplasia.

AUTHORS' SUMMARY.

COELIAC DISEASE. MARGARET EMSLIE, Proc. Roy. Soc. Med. **21**:563 (Feb.) 1928.

Emslie reports the case of a girl, aged 4 years, who had been healthy until the age of 1½ years, when she had whooping cough. From that time on she began to get thin and to show marked abdominal enlargement. Her stools became loose, frothy, bulky and offensive; they were light putty in color and were often mixed with undigested food. She was put on a high protein, fat-free diet and given cod liver oil. She improved on this diet.

WILLIAMSON, New Orleans.

DIARRHEA AND ENTERITIS IN PORTO RICO. E. B. PHELPS, Porto Rico Rev. Pub. Health & Trop. Med. **3**:345 (March) 1928.

The group of diseases classified as diarrhea and enteritis in the vital statistics of Porto Rico is the principal cause of death in the island. It is a disease of infants, for the most part, but is less sharply associated with the first year of life than is the disease of the same title in the continental United States. The time trend of the death rate under 2 years was steadily upward from 1910 to 1917, and has since been steadily downward. This is distinctly opposite to the time trend of typhoid fever. Seasonally, the distribution differs somewhat, as between the age groups under 2 years and over 2 years. In both there is a distinct association between seasonal death rates and normal rainfall. In the younger age group under 2 years, the association with rainfall is somewhat obscured by association with temperature, a feature which likewise characterizes the disease in the continental United States.

SANFORD, Chicago.

IRRADIATED ERGOSTERIN. A. HOTTINGER, Deutsche med. Wchnschr. **53**:1549, 1927.

The author reports the use of irradiated ergosterin in rickets and allied conditions. Following experimental work on rats and dogs, it was used in fifteen infants with florid rickets. In all these healing took place as rapidly as when irradiated milk was given, i. e., in from four to six weeks; tetany disappeared within from eight to ten days, and the blood phosphorous rose to normal within fourteen days. The dose for infants under 1 year is 1 mg. a day and for older infants, from 2 to 3 mg. Four adults were similarly treated; one was suffering from late rickets and tetany and three from osteomalacia. All showed remarkable improvement. The dose for adults is from 3 to 5 mg. daily.

RICKETS AND ITS MODERN TREATMENT. E. WIELAND, Fortschr. d. Med. **45**:1 (June 30) 1927.

The author gives an excellent correlation between the clinical appearance and course of rickets and the underlying pathologic changes as shown by the roentgen ray and blood chemistry. He also gives a comprehensive view of how the different antirachitic measures act in producing an active antirachitic substance. The following facts are emphasized: The first symptom of rickets, "craniotabes," does not appear before the third or fourth month, and the softness of the cranial bones in many new-born infants (the so-called "Angeborene Weichshadel" Wieland) should never be considered as a rachitic manifestation. Rickets is never congenital, although a predisposition toward it may be, and it certainly occurs more readily in premature than in full-term infants. It has been the experience in the Basel Clinic that the appearance of rickets in premature infants with a birth weight under 2,000 Gm. could not be prevented either by the direct or indirect use of the antirachitic factor.

LESLIE, Evanston.

MODERN TREATMENT OF RICKETS. R. WAGNER, Wien. klin. Wchnschr. **41**:438 (March 8) 1928.

Wagner regards the appearance of craniotabes as practically sufficient for the early diagnosis of rickets. He states that the roentgenogram is of chief value for demonstrating healing and in the investigation of the experimental disease. He has found Warkany's microchemical modification of the Doisy-Bell method for estimation of blood phosphorus to be simple and accurate enough for routine clinical use.

The author never employs more than 10 Gm. of cod liver oil daily in the treatment of infants with rickets. If young infants tolerate the pure oil poorly, he uses a 50 per cent emulsion prepared with Iceland moss and sugar. Infants with moderately severe rickets are cured by cod liver oil in six weeks. He also recommends irradiated stearin (ergosterin) in daily doses of from 12 to 25 minims (0.74 to 1.54 cc.) of a 1 per cent solution in olive oil. The experiences thus far at the Universitäts-Kinderklinik indicate that ergosterin does not heal rickets quite as rapidly as the methods hitherto employed.

Antirachitic therapy with the quartz lamp is used at the clinic according to the following plan: The distance of the lamp is maintained at 80 cm. The initial exposure is two minutes; this is gradually increased to a maximum of fifteen minutes, which is equally divided between the anterior and posterior surfaces of the body. Treatments are given three times weekly for a period of from two to three months. Wagner employs natural sunlight when it is available, according to the same scheme of time exposure that is used for the quartz lamp.

The author is of the opinion that there is little value in using window glass that it permeable to ultraviolet rays in cities for the control of rickets, since dust and smoke prevent the passage of most of the rays. He regards artificially activated milk to be of value in the prophylactic, but not in the therapeutic, control of the disease.

OLMSTED, Seattle.

Prenatal Conditions

PROBLEM OF THE CHILD WITH HARELIP AND CLEFT-PALATE. J. D. MCEACHERN, Canad. M. A. J. **18**:170, 1928.

The important points emphasized in this review of the subject are:

1. Closure of defect in the alveolar arch as early as possible, preferably at 3 weeks. The author also advises closure of the lip at this time.

2. Closure of the palate by the time the patient has reached the age of 2 years.

Satisfactory anatomic results can be obtained in from 80 to 90 per cent of the cases.

If the palate is closed before the child has learned to talk and a good anatomic result obtained, the functional results so far as speech is concerned are usually good.

MOORE, Omaha.

1. CONGENITAL ABNORMALITY OF CERVICAL VERTEBRAE. 2. CONGENITAL COCCYDINIA OR MEGALOCOCCYX. T. TWISTINGTON HIGGINS, Proc. Roy. Soc. Med. **21**:224 (Dec.) 1927.

1. After a normal birth, an infant, aged 6 weeks, was noticed to have a sharp projection on the spines of the lower cervical vertebrae, and over this projection there was a well marked dimple in the skin. Roentgenograms showed a hook-like process of bone in relation to the spinous processes of the fifth, sixth and seventh cervical vertebrae. Later, removal of these processes would be called for.

2. A girl, aged 5 years, had never been able to sit down with comfort. On examination, there were obvious signs of pressure in the skin overlying the tip of the coccyx. There was a postanal dimple, and the coccyx itself was prominent. The roentgenograms showed the upper two segments of bone ossifying, but the exact extent of the cartilaginous portion was only dimly shown in the negative. The author thought it possible that the condition might be due to some developmental error in connection with the closure of the neurenteric canal.

WILLIAMSON, New Orleans.

STENOSIS OF THE DUODENUM. V. VEAU and G. L. HALLEZ, Nourrisson **15**:244 (July) 1927.

This infant was well for twenty days after birth, when vomiting began. The yellow color of the vomited material permitted one to localize the obstruction. This was corroborated by the roentgen-ray examination, which placed the obstruction in the third portion of the duodenum. At operation, the upper two thirds of the duodenum were found greatly distended because of a compression by the mesentery. The muscle of Treitz was divided and the constriction relieved. The infant recovered and remained well for almost two months, when symptoms of intestinal obstruction appeared, and the infant died before surgical relief could be given. The postmortem examination showed the presence of a new peritoneal band behind which a loop of intestine had become strangulated. The authors believe that this could have been avoided if at the time of operation the opening in the peritoneum had been closed with a catgut suture.

MCCLELLAND, Cleveland.

CONGENITAL ATRESIA OF INTESTINE. ALFRED TOBECK, Virchows Arch. f. path. Anat. **265**:330, 1927.

Tobeck makes two cases of congenital atresia of the intestine the basis of a discussion of the genesis of this condition. In the first case the small intestine contained three areas of occlusion and the large intestine one; and in the second case there was a membranous occlusion at the junction of jejunum and ileum. The author does not accept fetal enteritis or amniotic adhesions as cause for the anomaly, but considers it the result of embryonic maldevelopment within the intestinal tract itself. Atresia occurs most often at those situations in which hyperplasia of the epithelium and mesodermal abnormalities of growth arise during fetal life, as determined by Tandler, Kreuter, Forssner and others. In both of Tobeck's cases partly calcified meconium bodies were present in the intestinal lumen below the sites of occlusion. Their presence can be explained only by assuming that the anomaly arises as a stenosis which permits the passage of material until after the secretion of bile is established. Complete occlusion is then followed by deposition of calcium, the calcium being excreted by the intestinal epithelium.

CLOACAL MALFORMATION. ALFRED TOBECK, Virchows Arch. f. path. Anat. **265**: 354, 1927.

The maldevelopment described, which occurred in a full term female child who died during delivery, consisted of a greatly distended vaginal cloaca into which the urinary bladder and rectum opened. The cloaca did not open to the exterior. The uterus was duplicated and consisted of two outpouchings at the upper pole of the cloaca. The ovaries were absent. Other anomalies noted were a biventricular trilocular heart and absence of the gallbladder. The peritoneal surface of the malformed urogenital organs was covered by a layer of fibrinous exudate. The peritonitis was a later condition than the maldevelopment and had no part in the causation of the latter. Cloacal anomalies of the type described are not the result of simple inhibition of growth and differentiation during the fetal period, but are due to a more complex combination of processes consisting of mesodermal hypertrophy at the region of the anal membrane, inhibition of growth of tissues immediately above this zone and overgrowth of the higher structures.

O. T. SCHULTZ.

ANOMALY OF CERVICAL VERTEBRAE. R. SIMON, Zentralbl. f. Chir. **54**:3247, 1927.

The cervical vertebrae, including the atlas, were fused in a solid mass (Klippel-Feil's disease).

ARACHNODACTYLIA. R. GANTHER, Ztschr. f. Kinderh. **43**:724 (July) 1927.

In arachnodactylia there is a remarkable congenital malformation of the skeleton which is distinguishable by a great increase in the length of the fingers and toes, especially of the distal phalanges. Since Marfan described such a case in 1896, only eight others have been reported. The peculiar slenderness of the fingers and toes was present in all of these patients at birth and must have begun early in fetal life. An injury to the endocrine system, especially the hypophysis, has been suspected as a cause, but there has not been a confirmation of this by anatomic observations. The patient here described weighed only 28 pounds (12.7 Kg.) at the age of 6¾ years. She walked stiffly and if she fell down could not get up alone because of the great weakness and awkwardness of her arms and legs. Her back was markedly deformed on account of a kyphos which began at the age of 9 months and had slowly grown worse. The expression of her face was that of an old person, while her skin was atrophied, waxy and moderately yellow and her hair was thin. The child was stiff at birth and hard to revive; it was noticed then that the fingers and toes were long and dry. From the first, whether on breast milk, on the bottle or on any other food, she vomited frequently until she was 3 years old. Her first teeth appeared at 18 months, and she did not walk until she was 30 months old. She had a dolichocephalic head, and roentgen-ray examination showed the sella turcica to be deep; sclerosis of the bones at the base of the skull also was present, but nowhere was there any sign of rickets or osteoporosis or periostitis. At the sixth month of pregnancy, the mother had a severe attack of grip, and it is thought that at this time an injury occurred to the embryo which resulted in the present malformation.

EMERSON, Boston.

Diseases of the New-Born

THE CEREBROSPINAL FLUID OF THE NEW-BORN. R. WAITZ, Rev. franç. de pediat. **4**:1, 1928.

This study is based on 300 successive lumbar punctures in new-born infants. Cerebrospinal fluid was not obtained in 249 instances; in the 51 cases in which it was obtained, the fluid was considered pathologic. In about half of these the fluid appeared clear, but contained increased albumin and cellular elements, not

leukocytes, but endothelial and reticular cells. The author feels that such fluid is a manifestation of an acute edema of the meninges. In the other cases, some hemorrhage was present in addition. By the fifteenth day the author was no longer able to obtain fluid by lumbar puncture except in those patients in whom hypersecretion persisted. There were two such patients, both of whom developed an external hydrocephalus. Forty-four autopsies were performed. One patient did not show cerebromeningeal lesions, nor had any fluid been obtained by lumbar puncture. In another case in which the presence of cerebromeningeal lesions was questionable, a few drops of fluid had been obtained. The other forty-two cases showed definite lesions, and in all of these fluid of the character mentioned had been obtained. From his study the author concludes that one does not obtain cerebrospinal fluid by lumbar puncture in the normal new-born infant. This differs considerably from the work of Sharpe and Maclaire, who, in a series of 500 consecutive cases, failed to obtain fluid in only 36 instances. LESLIE, Evanston.

AN UNUSUAL CASE OF CONGENITAL DEFORMITY OF THE EXTREMITIES. SARATOW NICHAMKINA, Monatschr. f. Kinderh. **38**:193 (Jan.-Feb.) 1928.

Nichamkina reports the case of a child born with congenital absence of the arms and legs. The upper extremities were stumps in which the humerus was present. There was no trace of bone in the lower extremities. The etiology is, of course, unknown. The mother came from the very poorest surroundings.

The child is still living at the age of 11 months. GERSTLEY, Chicago.

Acute Infections

THE SUSCEPTIBILITY OF FOWLS AND REPTILES TO THE VACCINE VIRUS. H. B. ANDERVONT, Am. J. Hyg. **7**:804, 1927.

It is shown that newly hatched white Leghorn chicks are more susceptible to the vaccine virus than full grown chickens of the same variety. By utilizing this observation, we are able to demonstrate the correctness of earlier observations, i. e., that the fowl responds to infection with the vaccine virus by the production of Guarnieri bodies, that newly hatched chicks are susceptible to cutaneous, corneal and intracranial inoculation of the neurovaccine virus, and that serial transmission of the neurovaccine virus through four chick brain passages can be accomplished. It is also shown that the vaccine virus can be carried through a series of three passages on the skin of turtles, aged 2 months. Typical Guarnieri bodies are observed within the skin and corneal lesions. These experiments show that the vaccine virus is capable of infecting animals of the order *Reptilia*. AUTHOR'S SUMMARY.

INVESTIGATION OF THE CATAPHORESIS OF TOXIN AND ANTITOXIN IN THE "FIELD AND TEAGUE" AND IN OTHER APPARATUS. M. E. MAVER and I. S. FALK, J. Immunol. **14**:219, 1927.

Maver and Falk have repeated the experiments of Field and Teague, using their apparatus. Both toxin and antitoxin migrate to the cathode. Numerous natural and purified proteins were also found in the cathode agar arc when electrolyzed in solution alkaline to their iso-electric points. The authors conclude from their experimental evidence that misinterpretation of the results obtained with their apparatus led Field and Teague to conclude that toxin and antitoxin are electropositive colloids. The results of an investigation of their apparatus support the explanation that the toxin and antitoxin do not migrate to the cathode by virtue of a positive charge which they carry, but that they are swept to the cathode by the endosmotic streaming of the water. When a U-shaped cataphoresis apparatus was used, the antitoxin migrated to the anode in solutions of p_H 12.5, 9, 8.2 and 6, and to the cathode in solutions

of p_H 4.6 and 3.8. Antitoxin may therefore be considered an amphoteric colloid. The toxin migrated to the anode in solutions having a p_H of 9.2, 8.2 and 6.6. But the toxin was more sensitive to acidification, and the potent toxin did not migrate to the cathode or anode at a p_H of 4.9 or 4.2.

S. A. Levinson.

A Study of Diphtheria Antitoxic Serum of Exceptionally High Potency with a Comparative Analysis of Its Various Constituents. M. B. Kirkbride and P. P. Murdick, J. Immunol. **14**:235, 1927.

Diphtheria antitoxic serums of exceptionally high potency, namely, 2,050 units per cubic centimeter, and of low potency, 230 and 290 units, and normal horse serum were analyzed to determine quantitatively their inorganic and organic constituents. The comparative analysis of the inorganic constituents yielded fairly constant amounts with only slight individual variations, excepting possibly in the content of calcium and of sulphur. A high calcium content was found in the more potent serum. In a second series of comparative analyses of six different serums, the results did not indicate a definite relationship although a later bleeding from the horse giving the highest titered serum, taken after the potency had decreased 750 units per cubic centimeter, showed a lower content of both calcium and sulphate than was previously obtained. Comparative analysis of the protein fractions showed a marked increase in the amount of pseudoglobulin in the antitoxic serums over that in the normal serum. This increase was especially noticeable in the serum of exceptionally high titer. The increase in pseudoglobulin was not accompanied by a decrease in albumin, but was entirely accounted for by the larger amount of total protein present. No significant changes in the euglobulin content were observed. The fats were present in fairly constant amounts both in the whole serum and in the globulin fraction.

Further Observations on the Specificity of the Green-Producing Diplococcus in Measles. Ruth Tunnicliff, J. Infect. Dis. **41**:267, 1927.

The green-producing diplococci isolated before the appearance of the rash in measles and during the acute stage of measles are immunologically distinct from nearly all similar cocci isolated during convalescence.

Measles cocci grown in normal and immune horse serum dextrose broth lose their specificity, as determined by the opsonic method. Their specificity may be restored by transferring them on blood agar at 36 C. for a few generations.

Growing measles cocci at room temperature does not affect their specificity, but growth at 40 and 41 C. completely removes their specificity as determined by the opsonic method.

Effect of Drying on the Specificity of Scarlet Fever Streptococci. Ruth Tunnicliff, J. Infect. Dis. **41**:272, 1927.

Scarlatinal streptococci, according to opsonic tests, lose their specificity through drying. This characteristic seems to be stable for about fifty generations, after being transferred on moist blood agar. The drying of streptococci may explain why streptococci isolated from walls and floors of rooms occupied by scarlet fever patients do not seem to belong to the scarlatinal group of streptococci.

Author's Summary.

The Etiology of Measles. Rudolph Gegkwitz, J. Infect. Dis. **41**:304, 1927.

The virus causing measles can be kept alive for several weeks outside the human system if blood of patients with measles is drawn just at the beginning of the rash and diluted in the proportion of 1:7 to 1:10 with buffered salt solution containing the same number of anions and cations and showing the same p_H as blood. This mixture must be kept at a temperature of 0 C.

Measles produced by inoculation in the skin begins earlier than natural measles or measles following an artificial infection of the mucous membranes of the respiratory tract; furthermore, the symptoms are milder and of shorter duration. There seems to be an analogy between morbilization against measles and variolation against smallpox.

Measles can be produced in human beings with material sterile from a bacteriologic point of view, with sterile blood of a patient with measles drawn at the right time, or with dilutions of such blood, which have passed through a Berkefeld filter. Sterile filtrates of nasal secretions collected in the pre-eruptive stage of the disease and diluted with physiologic sodium chloride solutions are also capable of producing measles.

Measles virus can be grown in vitro in culture mediums containing plasma from susceptible or immune persons which is diluted in a proportion of 1:6 or 1:7 with buffered physiologic sodium chloride solution. In order to keep the virus alive and to secure growth, it is necessary to associate it with living cells, such as slowly growing bacteria regularly found in cases of measles.

With sterile filtrates of cultures, reactions which are similar to measles can be provoked in human beings, the specificity of which can be proved by the fact that such persons are later immune against large amounts of infectious blood.

Monkeys *(Macacus rhesus)* can be made sick by injections of such material and the specificity of the reactions can be proved by the fact that their serum collected after the reaction can protect infected human beings against measles, while the serum of normal monkeys does not.

THE INCIDENCE OF SCARLET FEVER STREPTOCOCCI IN THROATS OF DIPHTHERIA PATIENTS. PAUL S. RHOADS, J. Infect. Dis. **41**:377, 1927.

Cultures of hemolytic streptococci were made from the throats or noses of 29 of a series of 100 patients who were admitted with the diagnosis of diphtheria to hospitals for contagious disease in Chicago.

Sixteen, or 55.2 per cent, of these strains of hemolytic streptococci were identified as scarlet fever streptococci by the toxin neutralization method.

The strength of the scarlatinal toxin produced by these strains varied from 100 to 10,000 skin test doses per cubic centimeter. It was less than 2,000 skin test doses per cubic centimeter in 14 of the 16 strains.

Thirteen, or 44.8 per cent, of the strains of hemolytic streptococci isolated did not produce any demonstrable scarlet fever toxin.

TETANUS FOLLOWING VACCINATION AGAINST SMALLPOX, AND ITS PREVENTION: WITH SPECIAL REFERENCE TO THE USE OF VACCINATION SHIELDS AND DRESSINGS. CHARLES ARMSTRONG, Pub. Health Rep. **42**:3061, 1927.

1. Epidemiologic evidence is presented which indicates that postvaccination tetanus, when it develops, tends to follow severe primary vaccinations performed with large insertions and dressed with some type of shield or covering strapped to the site.

2. Shields and dressings are shown markedly to predispose to the development of postvaccination tetanus in monkeys and rabbits vaccinated with virus artificially contaminated with *B. tetani.*

3. A proper vaccination is defined as one in which the insertion is not over one-eighth inch in its greatest diameter, made by some method which does not remove or destroy the epidermis. Such insertions treated openly, i. e., without the use of shields or dressings strapped to the site, have never, so far as we are aware, been followed by postvaccination tetanus. It seems probable that the adoption of these simple procedures of technic on the part of vaccinators, coupled with a proper warning to the person who was vaccinated, or his parents or guardian, concerning the dangers of home-applied shields and dressings, would eliminate tetanus as a complication of vaccination. ARCH. PATH.

DIPHTHERIA TOXOID-ANTITOXIN FLOCCULES. A. T. GLENNY and C. G. POPE, J. Path. & Bact. **30**:587, 1927.

Toxoid-antitoxin floccules are as good antigens as toxin-antitoxin floccules. The use of toxoid frees the preparation from all possible danger of increase in toxicity. The antigenic efficiency of the floccules is increased by heating to 80 C. for one hour.

HEMIPLEGIA FOLLOWING SCARLET FEVER. J. D. ROLLESTON, Proc. Roy. Soc. Med. **21**:213 (Dec.) 1927.

A boy, aged 3½ years, developed right hemiplegia and aphasia twenty-three days after a severe attack of septic scarlet fever. About a fortnight before the onset of the hemiplegia, there had been signs of a grave cardiac condition. Evidence of nephritis was not present. He gradually recovered power in the right arm and entirely regained the power of speech. He walked fairly well, with a slight scythelike movement of the right leg. In 1908, the author collected reports of sixty-six cases of this rare complication of scarlet fever, including three of his own. Since then only nine cases have been recorded. The foregoing case was only the fourth the author had seen and came after an interval of twenty years.

WILLIAMSON, New Orleans.

NASAL DIPHTHERIA. M. CHEVALLEY, Nourrisson **15**:213 (July) and 257 (Sept.) 1927.

A unilateral serosanguineous nasal discharge causing an erosive lesion of the upper lip is supposed to characterize this disease in infants. The author reminds one that scrofula and syphilis can do the same thing and at times "more abundantly." That some new-born infants are susceptible to nasal diphtheria is proved by numerous small epidemics reported from maternity hospitals. This type in young infants is relatively benign and may persist for weeks or months without serious consequences. The usual sequelae are infrequent; bronchopneumonia is the most serious complication and this is usually due to secondary invaders. Of 1,000 infants aged less than 1 year, 10 per cent were hosts of virulent *B. diphtheriae*. This incidence parallels the potential incidence as determined by a positive response to the Schick test.

The proper handling of these cases requires a nice discrimination. Attempts actively to immunize young infants have not been attended with success and are fraught with some danger. Experience has taught that it is not safe to abandon these patients to nature, because their congenital immunity may rapidly disappear. Although many are refractory to the effects of antitoxin, it should be given in preference to nonspecific protein therapy. In this way it is hoped that the virulent bacilli can be effectively overcome in many of these cases.

MCCLELLAND, Cleveland.

RUBELLA IS NOT ALWAYS BENIGN. P. CARRIEU, L. LAMY and P. BOUCHET, Presse méd. **36**:274 (March 3) 1928.

In a series of twenty cases of rubella, three terminated fatally. In the majority of the cases, the incubation period was established as sixteen days. About two thirds of the cases were light, but in the remainder the temperatures ran as high as 40.5 C. (104.9 F.). In two children adenopathies went on to suppuration. The deaths occurred in two cases in children of 4½ and 5½ years, respectively. Both deaths occurred on the third day with convulsions. The third death was that of a girl of 20 years.

SANFORD, Chicago.

ANTIDIPHTHERITIC VACCINATION WITH DIPHTHERIA TOXIN DETOXIFIED BY HEATING AND ADDITION OF SOLUTION OF FORMALDEHYDE. GUISEPPE SORGE, Riv. di clin. pediat. **25**:791, 1927.

The author used diphtheria toxin detoxified by heating and the addition of solution of formaldehyde, prepared by the Pasteur Institute of Paris to immunize subjects against diphtheria. Two injections immunized 77.7 per cent and three injections immunized 100 per cent of the thirty-six patients. Immunization was not found to result from the Schick test itself, even when it was repeated five times.

HIGGINS, Boston.

IS THE SCHICK TEST A PRACTICAL MEASURE OF IMMUNIZATION AGAINST DIPHTHERIA? H. OPITZ, Klin. Wchnschr. **6**:1701, 1927.

A single injection of toxin in the amount used with the Schick test stimulates antibodies. Therefore, the intracutaneous testing of diphtheria toxin is not suited for determining an immunization procedure. A further opportunity for error lies in the use of attenuated toxin solutions, which does not cause any skin reaction and, therefore, may suggest an established immunity. Toxins for the Schick test should be titered at the place where they are being used.

AUTHOR'S SUMMARY (ARCH. PATH.).

PERORAL IMMUNIZATION WITH KILLED B. DIPHTHERIAE. W. POCKELS, Klin. Wchnschr. **6**:2137, 1927.

Twenty-eight of thirty-two children were rendered "Schick-negative" in from four to seven weeks by the oral administration of killed diphtheria bacilli. The immunity is only slight. Possibly the tissue immunity is greater.

E. F. HISCH.

THE VIRUS OF MEASLES. R. DEGKWITZ, Klin. Wchnschr. **6**:2364, 1927.

The virus of measles can be kept alive in vitro if blood from a patient taken at the onset of the eruption is added to a physiologic sodium chloride solution of the same anion, cation and p_H concentration as the blood, in the proportion of 1:7 to 1:10 and kept at 0 C. Experimental infections can be produced with material that bacteriologically is sterile. Sterile filtrates of nasal secretions obtained in the prodromal stages of the disease, diluted and passed through a Berkefeld filter, have the same effect. The virus can be grown in the incubator on culture mediums consisting of plasma from susceptible people diluted with the described saline solution in the proportion of 1:6 to 1:7. To keep the virus alive and make it grow, living cells must be added or a small number of symbiotic slow growing bacteria. With sterile filtrates of such inoculated cultures reactions like measles can be produced in susceptible people, and specificity is demonstrated in that these persons become immune against large doses of the original infectious material. Monkeys *(Macacus rhesus)* are susceptible and the specificity of the disease is manifested in that their convalescent serum protects human beings, while normal serum fails.

OLMSTED, Seattle.

MENINGITIS PAROTIDEA. LUDWIG FABIAN, Monatschr. f. Kinderh. **38**:210 (Jan.-Feb.) 1928.

During an epidemic of mumps, three children, aged 7, 6 and 4 years, respectively, developed the clinical picture of meningitis. The results of examination of the spinal fluid and course of the disease were like those of tuberculous meningitis. In all three cases, however, recovery occurred.

POSTGRIPPAL NEURITIS IN EARLY CHILDHOOD. MAX FRANK, Monatschr. f. Kinderh. **38**:215 (Jan.-Feb.) 1928.

During an epidemic of grip, a number of children, after recovering from the febrile process, developed paralyses of the extremities. The spinal fluid was normal. In all cases recovery occurred.

The condition differred from poliomyelitis in that the paralyses did not develop until some time after the temperature became normal and the spinal fluid also did not show any change. Hyperesthesia never occurred, and in contrast to poliomyelitis the deep reflexes never disappeared entirely. The author is inclined to agree with the French pediatricians who believe these cases to be peripheral forms of epidemic encephalitis.

GERSTLEY, Chicago.

PREVENTION OF SCARLET FEVER. CARL LEINER, Wien. klin. Wchnschr. **41**:279 (Feb. 23) 1928.

During 1926, Leiner used specific methods for the prevention of scarlet fever in a children's hospital and thereby reduced the number of accidentally contracted cases to one third of those in the preceding year. For active immunization he employed a total of from 8,000 to 10,000 skin test units of toxin (3,000 units in children under 3 years), given in three doses at five day intervals. Ninety per cent of the children became negative to the Dick test in from ten to fourteen days. Although he himself has not seen any ill effects due to the toxin, Leiner mentions that Knopfelmacher and Nobel reported the occurrence of collapse following a large dose. Leiner believes that the duration of the active immunity is eighteen months. He states that in Poland rapid active immunization against scarlet fever has been accomplished by injecting a single dose of toxin previously treated with formol (anatoxin).

The author also reports the successful passive immunization of scarlet fever contacts in children's wards by Moser serum (antiscarlatinal streptococcus serum). Disinfection of rooms was abandoned. The serum did not cause harmful reactions.

ETIOLOGY OF MEASLES. B. LIPSCHÜTZ, Wien. klin. Wchnschr. **41**:365 (March 15) 1928.

Acting on the assumption that measles is caused by a filtrable virus, Lipschütz determined to search for characteristic changes in the cells of patients with measles. He stated that other infectious diseases of ultramicroscopic origin have been found to present specific cytopathologic pictures. Proceeding from the work of Mallory and Medlar, who have shown specific changes in the measles roseolum principally affecting the corium and secondarily the epidermis and the cutaneous lymphatic and glandular systems, Lipschütz investigated the cytology of these lesions. By means of hematoxylin and iron hemotoxylin stains he demonstrated within certain swollen cells isolated or conglomerated granules in the protoplasm. These characteristically staining cell inclusions were found in the corium and in the epidermis also in and around the hair follicles. Some of them displayed a diploid form, others were spherical and twice as large as the cell nucleus.

The author regards these granules as a hypertrophic form of cytoplasmic centers (Mikrocentrum), first described by Zimmermann, Heedenhain, et al. He has named the cells containing these elements "centrocytes," and he believes that they are pathologic. He did not find centrocytes in control material (syphilis, tuberculosis, typhoid roseolum, etc.). He was unable to produce the cutaneous lesions of measles in rabbits by local inoculation of infected material. He did, however, demonstrate centrocytes in sections of skin taken from monkeys who had been experimentally inoculated with measles. He attributes the specific changes in the cells previously described to the effect of the virus or toxin of measles.

OLMSTED, Seattle.

EXPERIMENTAL INVESTIGATIONS ON ENCEPHALITIS AFTER VACCINATION. H. ALDERSHOFF and A. B. F. A. PONDMAN, Nederl. Tijdschr. v. Geneesk. **72**:1198, 1928.

In earlier publications, the authors mentioned the different hypotheses as to the cause of encephalitis after vaccination and according to their opinion, a bacterial contamination of the vaccine belongs to these. Experimental researches of Pondman in rabbits with filtrates free from germs seem to indicate that a gram-negative bipolar bacillus might play an important rôle in the etiology of this type of encephalitis. Analogous results were recently obtained by Pette, who described how rabbits treated with vaccine became sensitive to the invasion of a bipolar bacillus which occurs in normal rabbits as a harmless organism. The presence of these germs in the vaccine in a filtrable form could not be wholly excluded, and therefore a bacterially sterile vaccine from Gaillardo in Spain was used temporarily in Holland. This vaccine did not prevent the occurrence of postvaccinal encephalitis, and the use of this "neurolapin" is soon to be abandoned on ground of new experiments on rabbits. The authors are inclined to accept the view that in the etiology of postvaccinal encephalitis a toxin substance, probably formed in the skin and provisionally called "neurocidrin," plays an important rôle. Together with this toxin substance and vaccine virus, *B. bipolaris* would also be significant in the etiology. In connection with these conclusions, based principally on experiments in rabbits, it is of importance that the authors obtained a nearly pure culture of *B. bipolaris* from the nose swab of a child with postvaccinal encephalitis.

THE ETIOLOGIC DIAGNOSIS OF TYPHOID AND PARATYPHOID. J. J. VAN LOGHEM, Nederl. Tijdschr. v. Geneesk. **72**:1436, 1928.

In this clinical lecture the author discusses the difficulties met in making an etiologic diagnosis of diseases with fever, owing to a "secondary" infection from the intestinal tract. He reports in detail a case in which during life the diagnosis of paratyphoid B seemed to be certain, but in which the bacteriologic investigation after death demonstrated that it was a real case of typhoid with secondary invasions, first of paratyphoid B then of *Staphylococcus aureus*. This and the experience of others teach that secondary invasion with other germs can make the true etiologic diagnosis difficult.

In conclusion the author communicates the good results obtained in Holland with a new simple method of cultivating typhoid and parathyphoid bacilli, described for the first time in 1923 by Leon Muller.

S. VAN CREVELD, Amsterdam.

BLOOD CULTURES IN RHEUMATIC FEVER. L. SURANYI and E. FORRO, Orvosi hetil. **72**:1, 1928.

A small number of patients suffering from rheumatic fever in different stages were examined by means of blood cultures. The cultures were positive in more than half of the cases. In febrile cases, the positive cultures ran as high as in 78 per cent of the patients examined. Nearly all the cultures gave short chains of streptococci, and they all belonged to the nonhemolytic and viridans group. The authors think that under more favorable conditions, even a higher percentage of positive cultures could have been obtained.

ZENTAY, St. Louis.

THE QUESTION OF EARLY DIAGNOSIS OF MEASLES. A. LAOUTZ, J. Pediat. (Russian) **2**:209, 1927.

Hecker in 1911 and Moltchanoff in 1912 thoroughly studied this question. Hecker came to the following conclusions: The blood of children affected with measles shows typical changes not only in the period of rash but at the end of the period of incubation. Thus, changes which always occur from two to six days before certain symptoms (Koplik's spots, enanthems) give a

possibility for an earlier diagnosis in suspected cases. The changes are: (1) leukopenia; (2) the relative and absolute diminution of lymphocytes; (3) alterations in Arneth's formula and (4) diminution of the eosinophil cells. The author gives many figures of blood analysis of different authors and concludes that the majority of the authors have emphasized a characteristic picture of the blood at the end of the incubation period and during the premonitory period.

The author studied thirty-three cases in the clinic. Unfortunately, it was difficult to make definite conclusions, because in certain cases the measles occurred in children who had scarlet fever at the same time. But in most of the cases, the acute manifestations of scarlet fever had already disappeared when measles occurred. The observations were made on twenty-nine children between 1 and 3 years of age and on thirteen between 3 and 9. The average time of appearance of the Koplik symptom was 1.7 days before the rash. The average time for the leukopenia was 3.5 days. The average time of the appearance of the hyperleukocytosis was six days. Hyperneutrophilia appeared, on the average, seven days before the rash. The eosinophils disappeared from the blood in an average of 4.3 days. The author could not make any definite conclusions about the lymphopenia on account of the scarlet fever, which usually is accompanied by pronounced lymphopenia.

Conclusions.—1. The most reliable and constant symptom for diagnosis of measles is still the Filatow-Koplik spots.

2. The analysis of the blood in the incubation period of measles has a great scientific interest, bringing one nearer to the understanding of the more intimate reactions of the body during the infection. But practically, the method cannot have a wide application on account of the complicated nature and the minuteness of a series of systematic investigations.

3. Leukopenia, lymphopenia and neutrophilia are not only symptoms of a beginning of measles but are the consequence of complicated factors which influence the picture of the blood, and also probably the vegetative nervous system (as serum disease and German measles).

THE QUESTION OF THE COURSE OF MEASLES IN CHILDREN WITH SCARLET FEVER. A. B. VOLOVIK, J. Pediat. (Russian) **2**:247, 1927.

The course of measles and its clinical picture are now being thoroughly studied. But in mixed infections, measles and scarlet fever, the course that measles takes is not yet definitely known.

Some authors (Brudzinsky, Tiktin-Hausman) do not think that scarlet fever has any influence on the course of measles; some think (Hase, Rolli, Kien, Risel, Sokoloff) that measles after scarlet fever takes a more serious course; Heubner, Flesch and Claus, on the contrary, think that measles takes a mild course in mixed infections.

The author's material represents 127 cases of measles occurring during scarlet fever. Sixty-seven patients were less than 3 years of age and 60 above 3 years of age.

Conclusions.—1. Cases of measles occurring during infection with scarlet fever have a tendency to assume a serious aspect.

2. Severe cases of measles in patients with scarlet fever occur not only in infants but in children between 6 and 12 years old.

3. The percentage of cases of pneumonia in children with scarlet fever and measles is 47 per cent, much higher than in those with measles only, and it affects infants as much as older children.

4. The death rate is higher in children with scarlet fever and measles.

5. In the course of measles with scarlet fever the appearance of Filatow-Koplik spots is retarded (three, four or five days) and the eruption is retarded as well (sixth or seventh day). The retardation of the eruption is more frequent in serious cases of measles.

6. The serum of reconvalescents from measles, administered even in the proper time and in proper doses, does not always prevent the patient with scarlet fever from having measles; big doses of serum (from 7.5 to 10 cc.) usually cause light and abortive cases.

7. The severity and peculiarity in the course of measles in patients with scarlet fever are connected with the lowering of the general immunity provoked by scarlet fever and activation of measles virus by scarlet fever.

SEVERAC, Philadelphia.

Chronic Infections

SYPHILITIC MENINGITIS IN INFANTS AND YOUNG CHILDREN. J. W. AMESSE and W. W. BARBER, Am. J. Syph. **11**:544 (Oct.) 1927.

Four cases of syphilitic meningitis in children are reported because of the relative rarity of these cases in the literature. The ages of the patients were 3 months, 10 months, 3 years, and 6 years, respectively. The tentative diagnosis in three of the four cases was tuberculous meningitis, an error which probably occurs frequently. Three patients had positive Wassermann reactions of the spinal fluid; one had a negative Wassermann reaction, although there was a suggestive colloidal gold curve. In this connection the authors state that both complement-fixation tests of the blood and spinal fluid may be negative. Two of the patients died; one was discharged as unimproved; and the fourth was discharged after four days with considerable improvement (this being the case with the negative test of the spinal fluid). In addition to the case reports, a brief summary is given of the symptomatology and pathology of this disease.

ANDERSON, Philadelphia.

THE LYMPHADENITIS OF TERTIARY SYPHILIS WITH SURVEY OF LITERATURE AND REPORT OF THREE CASES. CLYDE L. CUNNER, Am. J. Syph. **12**:13 (Jan.) 1928.

The author calls attention to the fact that lymphadenitis of tertiary syphilis is little discussed in the textbooks and literature. He reports three cases and reviews eighty-six additional cases, six of which occurred in patients with congenital syphilis.

The glands most frequently involved are those of the cervical region and the next most frequent are those of the groin, this frequency of cervical involvement making the differential diagnosis of syphilis and tuberculosis an important factor. The adenopathy responded readily to treatment.

SODIUM THIOSULPHATE AND ITS THERAPEUTIC FIELD IN SYPHILIS. L. G. BEINHAUER, Am. J. Syph. **12**:55 (Jan.) 1928.

With the prolonged treatment of persons with syphilis by means of the heavy metals, toxic symptoms often develop. Sodium thiosulphate has been found of great value in combating this toxicity and in the prevention of its development.

The deleterious action of the arsenic, for example, is explained as follows: The activity of the autonomic nervous system is depressed, thereby decreasing the barrier activity of the cells of the liver and skin. A greater amount of the metal is allowed to enter the cell, and its excretory function is decreased, thus allowing an excess of the metal to remain in the cells. This in turn damages the tissue, causing dermatitis or jaundice. The thiosulphate passes through the same channels but stimulates rather than depresses the autonomic nervous system, thus inducing an elimination of both the metal and the thiosulphate. This property of the drug explains its value in the so-called Wassermann-fast case.

This treatment is most effective in the trivalent arsenicals, less so in the pentavalent organic compounds, and of the least effect in the inorganic poisonings. It is but slightly toxic; 2 or more grams may be given intravenously with safety.

It is most effective if given intravenously but is also effective when given by mouth. It is of little value if given per rectum and of no value subcutaneously. The optimum dosage is 0.5 or 0.6 Gm. per day intravenously in serious cases, and biweekly injections in the less severe intoxications.

Authors differ as to the efficacy of treatment when thiosulphate and arsphenamine are used simultaneously. The author advocates the use of thiosulphate following the treatment with the heavy metal as a prophylaxis against intoxication. For local irritation from the arsenicals, infiltration of the tissue with 2 cc. of a 10 per cent solution of thiosulphate gives immediate relief. This drug is not of value in preventing the nitritoid reactions so often seen.

SODIUM THIOSULPHATE IN WASSERMANN-FAST SYPHILIS. L. G. BEINHAUER and F. M. JACOB, Am. J. Syph. **12**:61 (Jan.) 1928.

The authors have treated twenty-eight patients with Wassermann-fast syphilis with sodium thiosulphate. Good results were obtained in the majority of the cases, the Wassermann reaction in 85.6 per cent of the cases being reduced in degree and becoming completely negative in 35.7 per cent.

Deleterious effects were not noted in any of the twenty-eight patients treated.

R. H. McBRIDE, Sioux City, Iowa.

THE RELIABILITY OF THE KOLMER-WASSERMANN REACTION IN PREGNANCY. ARTHUR WILLIAM STILLIANS, Arch. Dermat. & Syph. **17**:318 (March) 1928.

Approximately 7,000 pregnant women were studied by means of the Wassermann and a flocculation test. Of the positive Wassermann reactions, not more than 2.5 per cent (three cases) could be considered as possibly false. Falsely negative tests were found more frequently and more definitely. The flocculation tests did not show as great a tendency as the Wassermann to give falsely negative reactions. The Wassermann reaction has almost the same diagnostic value in the pregnant as in the nonpregnant woman.

CLINICAL STUDIES ON THE KAHN REACTION. JUI-WU MU and HARTHER L. KEIM, Arch. Dermat. & Syph. **17**:387 (March) 1928.

More than 100 patients with high temperature were studied by means of parallel Wassermann and Kahn tests. The tests were made at the height of the fever and repeated when the patients were afebrile. In only four instances were the reactions positive during the febrile period and negative later. In all four, the positive reactions were exceedingly doubtful. It is therefore concluded that the reactions gave specific results.

JEANS, Iowa City.

AN UNUSUAL CASE OF ASTHMA. R. LOVE-SMITH, Proc. Roy. Soc. Med. **21**:564 (Feb.) 1928.

Love-Smith reports a case of asthma in a boy, aged 11 years. He had frequent severe attacks; during and just after the attacks he had albuminuria, edema and high blood urea. Between attacks his condition was normal.

WILLIAMSON, New Orleans.

IMMUNIZATION OF THE NEW-BORN WITH B C G. B. IAKHNIS, Ann. de l'Inst. Pasteur **41**:1045, 1927.

The Ukranian Commission reports the results of their investigations thus far. Vaccinations with B C G do not appear to exert any immediate influence on the state of health of the child, on the temperature, digestive organs, development, or resistance to exogenous or endogenous infections. Vaccinated children not exposed to tuberculosis often give a tuberculin reaction of medium intensity; those exposed more often show a marked reaction. The latter group

probably are infected at an early age with virulent organisms. The Commission considers the results encouraging, but conservatively states that all possible correlation should be made between the development, morbidity and mortality in nonimmunized children and in those who receive treatment.

M. S. MARSHALL.

UNEQUAL MALFORMATIONS PROBABLY OF CONGENITAL SYPHILITIC ORIGIN. RAVAUT and MONNEROT DUMAINE, Bull. Soc. franç. de dermat. et syph. **35**:9, 1928.

Two cases are reported of partial absence and malformations of the nails of the hands and feet. The syphilitic origin of the condition was not proved but was plausible.

HIGGINS, Boston.

TREATMENT OF PATIENTS WITH TUBERCULOSIS OF THE BONES AND JOINTS WITH CALCIUM CHLORIDE INTRAVENOUSLY AND ULTRAVIOLET RAYS. C. CLAVELIN and A. SICARD, Presse méd. **36**:227 (Feb. 22) 1928.

Twenty-eight patients were treated with intravenous solutions of calcium chloride. In the first series, five injections of a 1 per cent solution, in doses of from 50 to 250 cc., were given, followed by a 1.25 per cent solution in the same doses. After a twenty day rest, the treatment was resumed with five injections of a 1.25 per cent solution in doses increasing from 50 to 250 cc., followed by five injections of a 1.50 per cent solution in the same doses. After the injections, which were made every second day, the patient was exposed to the ultraviolet ray, for thirty treatments. The results were considered satisfactory. Only one case of intolerance was observed. In four patients, there was a slight decrease in weight; in six the weight remained stationary and in seventeen there was an increase of from 2 to 9 Kg. Many fistulas stopped suppurating and healed.

SANFORD, Chicago.

SYPHILODERMA LUPIFORMIS. G. LANTERI, Arch. ital. di dermat. sif. **3**:3 (Oct.) 1927.

The author reports two cases of tertiary lesions in cases of congenital syphilis. In the first case, there was an ulcer which had destroyed the nasal septum and both nares. The patient was 21 years old, and the condition had been present for thirteen months. The second case was that of a child, aged 7, with scars and ulcers on the right side of the face and neck. In both cases, the clinical diagnosis had been lupus vulgaris. Antisyphilitic treatment cleared up the lesions in both patients.

THE BEHAVIOR OF THE SKIN REACTIONS TO TUBERCULIN IN TUBERCULOUS MENINGITIS AND IN MILIARY TUBERCULOSIS. G. GELMI, Riv. di clin. pediat. **25**:769, 1927.

The author found the tuberculin test (Pirquet) positive in 101 of 123 patients with tuberculous meningitis and miliary tuberculosis. The percentage of negative tests was much higher when done in the last three days of life (42 per cent) than when done earlier (15 per cent). The age of the children seemed not to have any bearing on the percentage of negative tests. The percentage of negative tests in the winter was seventeen, in the spring ten, in the summer thirty-nine, and in the autumn eighteen.

HIGGINS, Boston.

PREVENTIVE INOCULATION AGAINST TUBERCULOSIS WITH CALMETTE'S B C G. R. KRAUS, Ztschr. f. Immunitätsforsch. u. exper. Therap. **51**:230, 1927.

Kraus discusses the problem of immunity in tuberculosis and describes his experiments with the B C G. Contrary to Calmette's results, he finds that the

organism possesses a certain virulence for animals with the production of definite tuberculous changes. These areas remain localized, however, and heal readily; he did not succeed in passing the infection from one guinea-pig to another. Consequently, he feels that the cultivation of the B C G on bile mediums has definitely reduced its virulence, similarly to the virus fixé. The favorable results obtained by Calmette are due to the virulence of the B C G, rather than because it is avirulent.

PREVENTIVE INOCULATION AGAINST TUBERCULOSIS WITH CALMETTE'S B C G. F. GERLACH, Ztschr. f. Immunitätsforsch. u. exper. Therap. **51**:256, 1927.

Gerlach tested three strains of B C G against guinea-pigs, rabbits and goats and found that the organism is not completely avirulent, as claimed by Calmette and Guerin, but that definitely tuberculous lesions were produced, which, however, tended to heal spontaneously. Four plates show the gross and microscopic appearance of the lesions.

PAUL R. CANNON.

THE QUESTION OF THE EXISTENCE OF A FILTRABLE FORM OF THE TUBERCLE BACILLUS. A. CHARLOTTE RUYS, Nederl. Tijdschr. v. Geneesk. **72**:795, 1928.

In this article, the author reports the researches made, especially by French investigators, on deviating and filtrable forms of the tubercle bacillus and also communicates the results of her own experiments on this subject. She concludes that the communications of the French investigators do not yet prove the existence of a filtrable form of the tubercle bacillus. In her own experiments with forty-two guinea-pigs in which filtrates of material containing tubercle bacilli were injected, only one showed the picture of a typical pathogenic form of tuberculosis. In all other animals neither bacilli resembling tubercle bacilli nor tuberculous changes in the histologic investigation could be found. In thirty-seven guinea-pigs treated with material from the animals in which the filtrates were injected also, typical bacilli or a histologic proof of tuberculosis could not be found.

S. VAN CREVELD, Amsterdam.

Internal Diseases

VEGETATIVE ENDOCARDITIS DUE TO THE MENINGOCOCCUS. C. P. RHOADS, Am. J. Path. **3**:623, 1927.

A case of vegetative and ulcerative endocarditis due to the meningococcus is reported and the literature reviewed. The identity of the organism is proved, culturally and seriologically. Lesions of the myocardium resembling those seen in rheumatic fever were obtained.

A CASE OF PRIMARY MESENCHYMAL HEPATOMA WITH NECROPSY. NATHAN CHANDLER FOOT, Am. J. Path. **3**:653, 1927.

A case of multiple tumors, occurring in a boy, aged 4, is described from the clinical and pathologic points of view, the latter being stressed. The tumors simulate multiple granulomas, a possible tuberculous or syphilitic, but when examined more closely are found to be neoplastic. They are rich in reticulum and are found to invade almost all the periportal tissue of the liver. Similar cells and reticulum are found in the contiguous costal bone marrow, which are probably metastases to that tissue, although this is not proved. The nature of the growth is discussed, and it is concluded that it probably had its origin in the mesodermal primordium of the liver; the possibility of its being of epithelial origin has not been overlooked.

AUTHOR'S SUMMARY.

SUPRARENAL CARCINOMA WITH PUBERTAS PRAECOX IN YOUNG BOY. M. B. GORDON and E. J. BROWDER, Endocrinology **11**:265, 1927.

Gordon and Browder report the case of a boy, aged 3 years, who presented symptoms of pubertas praecox, the onset being noticed at the age of 9 months. He was of herculean build, had a mannish voice, acne, pubic hair, light mustache, external genitalia of a boy aged 16 years, and premature ossification. His mentality was somewhat below that of a child of his actual age. Autopsy showed a carcinoma of the left suprarenal gland which extended into the left suprarenal vein and inferior vena cava with metastases in the lungs. The right suprarenal gland and right suprarenal vein were absent. That portion of the left suprarenal gland not involved by the tumor showed a picture generally found at the time of puberty; the thymus showed involution; the thyroid contained colloid; the pancreas, pituitary and pineal glands were normal. The testes were immature and did not show any spermatogenesis.

ARTHUR LOCKE.

RUMINATION AND PERSONALITY DEVELOPMENT. P. J. TRENTZSCH, J. Nerv. & Ment. Dis. **66**:245 (Sept.) 1927.

The author declares that it is impossible to obtain an accurate insight into any person by cross section study only; he must be studied as a whole and "longitudinally." He records three cases of infants at a few weeks of age who demanded a considerable amount of attention. They were all subject to rumination. They possessed a special personality make-up even at this early age, sufficient to acquire nicknames from their nurses. Rumination should therefore be looked for in the study of neurotic cases.

H. H. HART, Greenwich, Conn.

INTERSTITIAL NEPHRITIS WITH INFANTILISM ACCOMPANYING PYELITIS. DONALD PATERSON, Proc. Roy. Soc. Med. **21**:214 (Dec.) 1927.

A case was reported in a boy, aged 4½ years, a twin. The complaint was failure to grow, frequency of micturition, polyuria and polydipsia, of one year's duration. The patient was undersized and weighed only 23 pounds (10.4 Kg.). The urine showed a trace of albumin, low specific gravity, 0.8 per cent of urea and was full of pus and *Bacillus coli*. The blood urea was 109.6 mg. per hundred cubic centimeters, and the urea concentration test showed poor elimination of urea. The heart was hypertrophied, with a soft systolic murmur at the apex. The boy was sent to a hospital for incurables but returned one year later. He was circumcised, after which he gained 3 pounds (1.4 Kg.). Roentgen-ray examination showed osteoporosis at the first admission and no change a year later. Results of further laboratory investigations made after his return are given in the report.

1. CONGENITAL HEART WITH RIGHT BUNDLE BRANCH BLOCK. 2. PYKNOLEPSY. 3. SUPRAPITUITARY TUMOR (?). BERNARD SCHLESINGER, Proc. Roy. Soc. Med. **21**:215 (Dec.) 1927.

1. A case was reported in a child, aged 4½ years. There was no enlargement of the heart, but there was a rough systolic bruit all over the precordium on Aug. 8, 1924. The child had frequent attacks of bronchitis until March, 1927, when he was admitted to the hospital with acute tonsillitis. Tonsillectomy was performed. On March 28, 1927, some enlargement of the heart was found. On Sept. 2, 1927, an electrocardiogram showed right bundle branch block. This condition is rare in children with congenital malformation of the heart; the author had been unable to discover any record of another case.

2. A girl, aged 8½ years, at the age of 6 years, began to have fits and would have from five to six an hour. The fits gradually became worse in character and more numerous. A diagnosis of pyknolepsy was made. The patient had had as many as fifty fits in one day. The history showed that other members in

the patient's family had suffered from similar fits. The disease apparently had been inherited from the paternal grandfather, although the child's father had escaped. Every method of treatment had been tried but without success. If the diagnosis is correct, however, the prognosis is good.

3. A girl, aged 9 years, had had a large head since birth, and recently, it had been increasing in size and was out of proportion to the size of the body. The circumference of the head was 24½ inches (62.2 cm.). Hydrocephalus, adiposity and optic neuritis were present. Increased knee and ankle jerks were present. Roentgen-ray examination showed the sella turcica to be enlarged, deepened and rounded, and the clinoid processes were not visible. The intelligence of the child was good. If this were a case of congenital hydrocephalus, there would be a decided impairment of intelligence. The optic neuritis which had developed during the last few months points rather to a secondary hydrocephalus with a cerebral tumor as the cause.

SPECIMEN: CONTRACTED GRANULAR KIDNEY WITH ADENOMATOUS HYPERTROPHY. J. HENRY DIBLE and H. CHODAK GREGORY, Proc. Roy. Soc. Med. **21**:219 (Dec.) 1927.

A girl, aged 8 years, was brought to the hospital complaining of a discharge from the ear which had been present intermittently for two years. There was a history of nocturnal incontinence until the age of 6 years. The child was well nourished, but small for her age. The face was pale and puffy. The heart was slightly enlarged and also the tonsils. The urine was scanty and contained much albumin, blood and a little pus. Three days after admission, the child had violent leftsided convulsions which later became generalized. Lumbar puncture gave temporary relief, but the child died seven days after admission. Postmortem examination showed hemorrhage into the frontal and occipital lobes on the right side of the brain. The right kidney weighed ¾ ounces (21.2 Gm.) and the left, 1¾ ounces (49.6 Gm.). The right was small and shrunken with whitish nodular growths, and the portions of tissue lying between had the appearance of extremely cirrhotic renal tissue. Both ureters were thickened, and the bladder showed considerable thickening of the muscular and mucous coats.

The report is accompanied by a detailed microscopic account, as well as drawings, of both macroscopic appearance and microscopic sections of the kidneys.

CASE OF ? CHLOROMA, ? SUPRARENAL TUMOR. REGINALD C. JEWESBURY, Proc. Roy. Soc. Med. **21**:229 (Dec.) 1927.

A boy, aged 1 year, was brought to the hospital because of a bruise of the eyelids and some prominence of the eyes, which had gradually come on during the past four weeks. On examination, bilateral proptosis and bulging of the eyes were found. The patient could not close his eyes during sleep. There was marked ecchymosis of the lids and also congestion of the conjunctiva. The fundi were normal; the pupils were equal and normal in size and to reaction to light. The skin was greenish, and the glands in the groins, axillae and neck were enlarged; the liver was enlarged. The blood showed: red cells 2,060,000; hemoglobin, 23 per cent; leukocytes, 20,600 with a lymphocytosis. Roentgen-ray examination of the bones showed nothing abnormal. The author felt that the picture of the child was suggestive of chloroma and the blood picture that of lymphatic leukemia, but he also thought that the condition might be primarily due to a growth of the suprarenals.

RENAL INFANTILISM. JAMES MAXWELL, Proc. Roy. Soc. Med. **21**:561 (Feb.) 1928.

Maxwell reports the case of a boy, aged 9 years, weighing 23¼ pounds (10.5 Kg.). The child had albuminuria.

WILLIAMSON, New Orleans.

ACRODYNIA IN THE INFANT AND THE ADULT. LUDO VAN BOGAERT, V. KOUMANS and J. SWEERTS, Rev. franç. de pediat. **4**:86, 1928.

After describing two cases of acrodynia in infants, the authors discuss a similar case occurring in an adult. Two months after a severe attack of grip, the patient, a girl, aged 20 years, developed a neurodermatologic syndrome, characterized by extreme asthenia, marked pain of the skin and muscles and an intense pruritis with trophic ulcerations. To this was added spasmodic constipation, urinary and gastric disturbances, and tachycardia with hypotension. A spontaneous cure occurred in the course of seven months. In addition to the similarity of symptoms, all three cases showed leukocytosis and, what is brought out for the first time in this paper, hyperglycemia with a lower amount of sugar in the cerebrospinal fluid. The cerebrospinal fluid also showed at times, but not consistently, a slight increase in albumin and cells. The authors feel that these manifestations, in addition to certain of the clinical phenomena, that is, the abolition of tendon and abdominal-cutaneous reflexes and a positive Babinski sign, suggest involvement of the central nervous system as well as of the peripheral system.

LESLIE, Evanston.

INDOXYLURIA IN CHILDREN. GUISEPPE HALFER, Riv. di clin. pediat. **25**:801, 1927.

Healthy adults ordinarily show between 1.5 and 1.9 mg. of indican per hundred cubic centimeters of urine, while normal children show from 0.2 to 0.7 mg. Normal infants, under 1½ years of age, seldom show indican reaction.

The quantity of indoxyl in the urine was found to be high (more than 1 mg. of indican per hundred cubic centimeters) in patients with tabes mesenterica, miliary tuberculosis, pulmonary tuberculosis and faucial diphtheria. The author did not find indoxyl in abnormal quantity in patients with enteritis, typhoid fever, paratyphoid fever, appendicitis, measles, pertussis or scarlet fever. Inconstant results were found in patients with nephritis, endocarditis and nervousness. In all, determination in 100 cases are reported.

HIGGINS, Boston.

A PAPILLARY MYXOMA OF THE RIGHT AURICLE. B. UGRIUMOW, Centralbl. f. allg. Path. u. path. Anat. **41**:7, 1927.

A girl, aged 15, died of cardiac decompensation. At autopsy, both leaves of the pericardial sac were grown together. The right auricle was almost entirely filled with papillary, grapelike clusters of red-gray, jelly-like material, over all, 7.5 cm. in diameter attached by a wide stalk to the site of the foramen ovale. Several papillae extended past the tricuspid ring and were attached to the leaflets and papillary muscles of the tricuspid valve. Microscopically, the centers of the papillary masses consisted of fresh blood surrounded by lymphocyte-like cells and a few plasma cells, but the stellate cells characteristic for a myxoma were not found.

GEORGE RUKSTINAT.

BLOOD GROUPING IN A HEMOPHILIC FAMILY. ANDÉAS KUBÁNYI, Klin. Wchnschr. **5**:321, 1926.

The studies indicating the heritable nature of blood groups suggests a possible relationship with hemophilia. A patient whose condition and family history indicate that he is hemophiliac, is found to belong to group 2 as do also his mother and sister. His healthy brothers belong to group 3.

ARCH. PATH.

INVESTIGATIONS OF THE BLOOD GROUPING IN THE HEMOPHILIC MAMPEL FAMILY OF HEIDELBERG. ANDRÉAS KUBÁNYI, Klin. Wchnschr. **6**:1517, 1927.

Investigations concerning the occurrence of hemophiliac persons in the Mampel family of Heidelberg, covering a period of more than 100 years, are briefly reviewed. A report of 1905 stated that of 207 members examined, 111

were men, and of these, 37 (33.33 per cent) were hemophiliac. In the present study of the blood grouping of thirty-seven members of this family (in four different branches), only groups 2 and 4 were found. Three of the four persons with hemophilia who were severely affected but survived belong to group 4; no nonhemophilic man belonging to group 4 was found; and the daughters of these families were all in group 2. The coincidence is noted that all the men who married into this family (so far as the study goes) belonged to either group 2 or group 4. Studies are planned for the children of the daughters in the present generation.

ETHEL B. PERRY.

CHEMICAL ANALYSIS OF THE SPLEEN IN LIPOID CELL SPLENOHEPATHOMEGALY (NIEMANN-PICK). B. BRAHN and L. PICK, Klin. Wchnschr. **6**:2367, 1927.

The spleen weighed 198 Gm., and chemically it contained per hundred grams moist weight, 15.1 total lipin, 1.39 cholesterol, 0.4 cholesterol ester and 10.3 lecithin. These results agree with other reports in the belief that the metabolic disturbance concerns the phosphatids. There is also relatively as great an increase of the cholesterol, and apparently also of the cholesterol esters.

E. F. HIRSCH.

ELECTROCARDIOGRAPHY IN THE DIAGNOSIS OF HEART DISEASE IN CHILDREN. THEKLA BUNGARTZ and HANS DRESSEN, Monatschr. f. Kinderh. **38**:202 (Jan.-Feb.) 1928.

The authors report a case of aortic stenosis in a child, aged 8 years, complicated by embolic processes in the vessels of the brain and heart. By means of the electrocardiogram, a diagnosis of embolus in the right bundle of Tawara was diagnosed.

NURSLINGS' DYSENTERY. S. ROSENBAUM, Monatschr. f. Kinderh. **38**:213 (Jan.-Feb.) 1927.

The author criticizes Leo Buchholz who, in volume 36, page 351, of the *Monatschrift*, described glycosuria as part of the picture of dysentery and thus of no value in differentiating dysentery from alimentary intoxication. Rosenbaum suggests that the patients in the cases of dysentery reported may have had an associated alimentary intoxication.

ALLERGY AND STROPHULUS. DORA KARPLUS, Monatschr. f. Kinderh. **38**:234 (Jan.-Feb.) 1928.

Using the method of skin testing the author studied twenty children with strophulus against a control group of twenty normal children. The control group showed entirely negative reactions. The strophulus group showed positive reactions in a majority of cases, to two or more extracts. Most of the positive results were obtained with fish protein and after that, with extracts of egg and milk. Susceptibility to dandruff was not present in any case.

GERSTLEY, Chicago.

TREATMENT OF EXUDATIVE PLEURISY WITH THE MERCURY QUARTZ LAMP. OTTO LASSEN, Ugesk. f. Laeger. **90**:220, 1928.

Eleven patients with exudative pleurisy are presented, and the beneficial effects from treatment with the mercury quartz lamp are shown by charts. In all cases there was a definite drop in the temperature to normal and simultaneously with this a general systemic improvement. In only two cases was aspiration necessary because of the large amount of fluid at the time of entrance. The author advocates that light treatment be started in the febrile period. The advantage of this treatment is that it materially shortens the period of hospitalization.

SCHLUTZ, Minneapolis.

EPIDEMIOLOGIC CONTRIBUTION TO THE KNOWLEDGE OF THE DISEASES OF THE RESPIRATORY ORGANS. J. J. VAN LOGHEM, Nederl. Tijdschr. v. Geneesk. **72**:665, 1928.

In these articles, the author communicated the results of an extensive epidemiologic investigation on mild diseases of the respiratory organs made in Holland between September, 1925, and July, 1926. The researches made by the Public Health Service in the United States (first publications by Townsend and Sydenstricker in 1927) and of Schade in Germany were known to the author. He made his inquiry about refrigerations and slight influenza, not among students, but nearly exclusively among heads of families (medical men, dentists, teachers, pharmacists and other intellectuals). The official inquiry was extended to about 7,000 persons. A report was given each week about an eventual refrigeration and its degree (by symptoms of coryza, angina, laryngitis, etc.). The results of the inquiry were not contradictory to the author's supposition that several diseases of the respiratory passages are caused by a disturbance of the regulation of the body temperature. In consequence of this, the body is sensitive to infection from organisms that it already harbors. The influenza manifested itself as a parasitic infection which runs its own epidemic course. This information gives support to the conception that cold promotes influenzal pneumonia. As under normal conditions the regulation of the body temperature is not complete, but a certain poikilothermism exists, as the author remarks at length, it is clear that with a marked decrease of the outside temperature, the fluctuations of body temperature may become so great as to cause disturbance.

The prophylaxis of refrigeration must consist of conservation of heat as well as increase of heat production of the body.

S. VAN CREVELD, Amsterdam.

HELMINTHIASIS IN SCHOOL CHILDREN. V. J. RABINOVITCH and A. M. KRASNOSHCHOKOVA, J. Pediat. (Russian) **2**:211, 1927.

Helminthiasis and all the questions in connection with it have become more and more important in recent years. The discovery of the phenomenon of the migration of the eggs of the worms through noninjured skin and their ability to infect the animal with bacteria in this way, and also the toxic effect of certain worms (ascarides) proved the danger of such an infection for the human being.

The authors examined 410 children in five different schools of Kharkov. In all children smears were taken from the perineum and examined; also, the feces were examined. In 175 children, smears were examined from the particles of dirt accumulated under the finger nails. Fülleborn's method of examination, which was used mostly, is based on the observation that eggs of the worm are lighter than water and float on its surface. The feces are thoroughly stirred and a salt solution added gradually so that to 1 part of feces 20 parts of salt solution are added. The feces are then left standing for one hour and fifteen minutes. During this time the eggs come to the surface of the fluid; then, with a platinum loop, a drop is carried from the surface and deposited on a slide.

Conclusions.—1. The method of examination for eggs in which a small quantity of feces is mixed with a small amount of salt solution and examined under the microscope is not satisfactory. This method gives 5 per cent less positive results than Fülleborn's method.

2. For mass examinations Fülleborn's method is convenient, simple and cheap and is not inferior in exactness to Telleman's method.

3. In mass examinations and in cases in which oxyuriasis is suspected, it is necessary to employ the method of taking smears from the folds of the perineum. With this method, one obtains positive results three times as often.

4. In 4.6 per cent of the cases, the eggs were found in material from under the nails.

5. The extent of the helminth invasion in school children of Kharkov from 7 to 14 years of age is 63.4 per cent (one examination of the perineum).

6. Helminthiasis is more frequent in boys (68.4 per cent) than in girls (58.8 per cent).

7. The type of worm which occupies the first place is *Oxyuris vermicularis*, 60 per cent, then *Trichocephalus dispar*, 46.9 per cent, *Taenia nova*, 14.2 per cent, *Ascaris lumbricoides*, 13.8 per cent. Mixed double or triple infestation in different combinations is 30 per cent; double, in 26 per cent and triple, in 4 per cent.

8. *Oxyuris vermicularis* is found almost in the same percentage in boys and girls (boys, 38 per cent; girls, 35.5 per cent). *Tricocephalus dispar* is found more often in girls—25.2 per cent, and in boys, 20.1 per cent. *Taenia nova* is found more often in girls (7.1 per cent) than in boys (3 per cent). The percentage of *Ascaris lumbricoides* is almost the same (4 per cent in girls and 6 per cent in boys).

9. Infestation with helminth is distributed almost evenly in the age interval of from 7 to 14 years.

10. The prolonged stay in school influences the propagation of the infestation with helminth.

11. Crowding favors the infestation with helminth. The percentage of infestation of children who live two in one room is 55.9 per cent; four children in one room gives a percentage of 70.3.

13. Playing with domestic animals assists the infestation.

14. Helminthiasis, even without manifestations which would provoke complaints from the infected child, should be considered as a disease which may become aggravated at any time.

15. Infected children should be considered as bacteria bearers, as a source of propagation of helminthiasis.

16. Without any particular clinical manifestations, helminthiasis often is a cause of children's undernourishment.

17. A prophylactic examination of all school children, children's homes, day nurseries and other institutions is necessary to determine the cases of infestation and to begin the campaign for elimination of helminthiasis.

18. Children entering any institution should undergo an examination for helminthiasis at the same time that they receive a prophylactic examination.

SEVERAC, Philadelphia.

Nervous Diseases

A MILK-BORNE EPIDEMIC OF POLIOMYELITIS. W. L. AYCOCK, Am. J. Hyg. **7**:791, 1927.

The distribution of cases of poliomyelitis in the Broadstairs epidemic, in point of time, indicates that the majority of persons were simultaneously infected. The data concerning the four patients who left Broadstairs before the epidemic, with a high degree of probability, fix a definite period of infection from which it may be inferred that the incubation period was in the majority of cases between six and fourteen days. The evidence concerning the milk supply points strongly to the milk furnished by one dealer as the common source of infection, and it further suggests that contamination of only one grade of his milk, which came from a single farm, was responsible for the epidemic.

AUTHOR'S SUMMARY.

THE SIGNIFICATION OF THE AGE DISTRIBUTION OF POLIOMYELITIS. W. L. AYCOCK, Am. J. Hyg. **8**:35, 1928.

In Vermont more cases of poliomyelitis occurred in the younger age groups in urban than in rural communities. The age distribution of measles, diphtheria

and poliomyelitis is of the same order, and the incidence of each disease in the various age groups is proportional to the concentration of the population. This fact indicates that the mechanism involved is similar for all these diseases. In poliomyelitis immunity, largely subclinical, is responsible for the age distribution. It appears that the virus of the disease is just as widely distributed as those of measles and diphtheria, and in the course of this distribution the majority of persons become immunized.

SYPHILIS AND EPILEPSY. HAROLD A. PATTERSON, Am. J. Syph. **12**:41 (Jan.) 1928.

From a study of his own cases the author believes the following conclusions to be justified: 1. In a group of forty-one epileptic patients with syphilis, the syphilis appeared much more frequently as an incidental than as an etiologic factor. 2. In those instances in which it did assume a causal rôle, the syphilis preceded the epilepsy; in those instances in which it seemed to occur as an incidental element, the syphilis was, as far as could be ascertained, likely to run its course independently of the epilepsy. 3. In those cases in which it may have been etiologic, antisyphilitic treatment seemed decidedly beneficial in ameliorating the resulting convulsive disorder. 4. When it was coincidental the effect of antisyphilitic treatment was dubious.

An analysis of the literature and of his own cases, in an epileptic colony, appears to point to the conclusion that the incidence of syphilis in epilepsy is less frequent than among the insane or the feebleminded, and that its occurrence probably does not exceed the rate obtained among the population as a whole.

ARCH. NEUROL. & PSYCHIAT.

COLLOIDAL GOLD: A METHOD FOR THE PREPARATION OF COLLOIDAL GOLD FOR THE LANGE TEST ON CEREBROSPINAL FLUID. S. L. LEIBOFF, Arch. Dermat. & Syph. **17**:380 (March) 1928.

A method is described for the preparation of colloidal gold solution with ordinary distilled water. The description also includes a method for titrating the solution so that it may be adaptable for the performance of the Lange test and give uniform results.

JEANS, Iowa City.

RELATION OF INFANTILE CONVULSIONS, HEAD-BANGING AND BREATH-HOLDING TO FAINTING AND HEADACHES IN THE PARENTS. D. M. LEVY and H. T. PATRICK, Arch. Neurol. & Psychiat. **19**:865 (May) 1928.

The frequency of periodic headache in groups of apparently normal women in five communities was as high as 40.2 per cent. These headaches were largely migraine. The frequency of fainting in apparently normal women was 28 per cent.

Parents who fainted or who had periodic headaches were more likely to have children who had infantile convulsions, temper with head-banging or breath-holding, and other recurrent attacks, especially spells of vomiting and fainting. Parents who fainted were more likely to have such children than parents who had periodic headaches but remained free from fainting. Parents who had periodic headaches were more likely to have such children than those whose headaches were infrequent. The same was true of fainting.

Conversely, children who had "explosive symptoms" were more likely to have parents who fainted and had periodic headaches than children who were free from such symptoms. The "explosive symptoms" — infantile convulsions, and temper with breath-holding — were in correlation with each other and with fainting and periodic headache in the parents.

SANFORD, Chicago.

NOTES ON THE MENTAL DEVELOPMENT OF CHILDREN EXHIBITING THE SOMATIC SIGNS OF PUBERTY PRAECOX. LOIE DOE-KULMANN and CALVIN P. STONE, J. Abnorm. Psychol. **22**:291 (Oct.-Dec.) 1927.

A review of available records of sixty-two cases leads to the conclusion that the rate of mental development is normal or subnormal, and seldom, if ever, accelerated. Specific trends of mental development are probably not closely correlated with specific types of pathologic development or with the possibility that functioning of the endocrine glands underlies the disorder. There is no evidence pointing to a distinctly hereditary basis.

HAMILL, Chicago.

PACHYMENINGITIS HEMORRHAGICA, AN EXPERIMENTAL STUDY. I. J. and I. K. PUTNAM, J. Nerv. & Ment. Dis. **65**:260 (March) 1927.

The authors studied pachymeningitis hemorrhagica in three ways: by the subdural injection of 2 cc. of blood; by examining patients dying after intracranial operations, and by feeding alcohol over long periods to animals. Five of eighteen cases did not show any membrane after blood injection; in all cases there was much less clot than might have been expected. One almost constant feature was that the mesothelial line spaces were usually empty or contained a little blood or debris. These lesions resembled the progressive lesions of pachymeningitis in appearance but not in behavior. Injection of irritating substances subdurally produced a fibrous scar with adhesions only. Specimens were taken from the preserved duras of eighteen patients dying at various intervals after intracranial operations. Rarely, a definitely pigmented scar was found but never a lesion of significant size. Experimental chronic alcoholism never produced a subdural membrane in dogs. Experimental studies thus throw little light on the progressive subdural hemorrhage shown by clinical and pathologic observation.

HART, Greenwich, Conn.

AN UNUSUAL CASE OF ACUTE ANTERIOR POLIOMYELITIS. RALPH P. SMITH, Canad. M. A. J. **18**:304, 1928.

A boy, aged 14 years, developed a sore throat while in swimming and, on leaving the water, an inability to swallow even fluids. He became comatose, with a rise in temperature, and died. Nothing was noted on physical examination. Postmortem examination showed the histologic changes of anterior poliomyelitis in the spinal cord.

MOORE, Omaha.

SUPRACLAVICULAR LESION OF WHOLE BRACHIAL PLEXUS. REYNOLD H. BOYD, Proc. Roy. Soc. Med. **21**:225 (Dec.) 1927.

A girl, aged 5 years, was run over by a car. She complained of pain in the neck and the left arm. A hematoma of the scalp was found on the left side above and ½ inch (1.2 cm.) anterior to the left auditory meatus. The left arm was limp, and movements could not be performed by the patient at the shoulder, elbow, wrist or finger joints. Flaccid paralysis of the left arm with loss of sensation to all stimuli was present. An intracerebral lesion was not found. Both pupils reacted to light and in accommodation, but the left was much smaller than the right. The arm was placed on a Fairbanks splint and given massage daily.

WILLIAMSON, New Orleans.

FACIAL NERVE PARALYSIS. D. W. WINNICOTT, Proc. Roy. Soc. Med. **21**:565 (Feb.) 1928.

Winnicott reports a case of facial paralysis in a child, aged 10 months. The child had been well previously. He became feverish and vomited twice. The next day right facial weakness was noticed. For two days, the infant slept

excessively. On the eighth day of the illness, he was admitted to the hospital; at that time there was a severe right facial paralysis. Lumbar puncture showed turbid fluid, globulin and 300 cells. An irregular temperature lasted three weeks. The facial paralysis gradually decreased, and further signs or symptoms did not develop.

FACIAL NERVE PARALYSIS ASSOCIATED WITH FITS. D. W. WINNICOTT, Proc. Roy. Soc. Med. **21**:566 (Feb.) 1928.

Winnicott reports a case in a boy, aged 7 years. In October, 1923, when he was 2 years and 11 months old, he had measles, followed by a fit. After the measles he had six more fits. The second fit occurred in November, 1923, the third fit in January, 1924, and the fourth, fifth, sixth and seventh fits, from February to August, 1924. About August, 1924, he developed left facial weakness.

WILLIAMSON, New Orleans.

ENCEPHALITIS AFTER MEASLES AND CHICKENPOX. D. W. WINNICOTT, Proc. Roy. Soc. Med. **21**:567 (Feb.) 1928.

The patient had been well till the age of 1 year and 9 months; she then had measles and chickenpox, and had not been well since. She seems to have no power of balancing; the attempt to balance brings about terror which makes apparent a respiratory difficulty.

"C. N. S. lesions are: 1st. Masklike expression. 2nd. Lack of balance. 3rd. Right vocal cord has only slight range of movement." Treatment by massage increased speed of recovery of function.

ARCHICAPILLARIES AND MENTAL DEFICIENCY. H. DELBRUECK, Arch. f. Psychiat. **81**:606 (Sept.) 1927.

The author reports the results of an investigation of the structure of the capillaries in children of different types (both mentally deficient and normal) along the lines suggested by W. Jaensch. The latter, following the work of O. Müller, claims that in a great majority of feebleminded children the end capillaries show a distinct deviation from the normal in the form of faulty development. Hoepfner gives a classification of these types of capillaries: The archicapillaries which tend to assume the shape of a horizontal network; these should disappear at the end of the first year, giving rise to the thin vertical capillaries of the normal child by going through a series of changes which are called intermediary types. Pathologically, either one of these primitive forms may be found at an age when they should have disappeared (giving place to the normal type) or the transformation may proceed along abnormal directions, developing all types of bizarre pictures. The studies are made by photomicrography of the capillaries of the fingers. The author has found most of the types described by Hoepfner, but he could not substantiate the relation of such occurrences to mental deficiency. He distinguishes five of the types described by Hoepfner: productive faulty development, intermediary, intermediary deviations, neurosis type and neocapillaries. Four hundred and fifty children were examined, some of them being school children of normal and superior intelligence, others of special classes for mentally deficient children.

The results could be summed up as follows: there were practically as many pathologic forms among the normal and superior children as among those belonging to special classes. Those that showed archicapillaries, both of the normal as well as of the mentally deficient children, did not show any difference in their intellectual faculties from those whose capillaries were of normal shape. An investigation of the relation between special neurotic manifestations and these pathologic capillaries shows no correlation between the two. Some

investigators suggest that pathologic capillary forms of this type are met with in children who show other stigmas of degeneracy. The author found no such correlation.

In his conclusions the author is of the opinion that although a pathologic maldevelopment of the capillaries, as suggested by Jaensch, does exist, the relation that they bear to mental deficiency, as suggested by this author, could not be substantiated.

CAPILLARY FORMS IN THOSE MENTALLY DEFICIENT AND THEIR RELATIONS TO PSYCHIC DEVELOPMENT. H. K. KAHLE, Arch. f. Psychiat. **81**:629 (Sept.) 1927.

The author reports an investigation of capillary forms in 507 inmates of an institution for feebleminded children as compared with a similar investigation of ninety-two normal school children. The investigation was conducted along the lines suggested by W. Jaensch. It was found that only five of the normal children showed abnormal capillary forms; all the others belonged to the normal groups. Three of the five were reputed to be backward children. The feebleminded children could be divided into three groups according to the capillary types: (1) The first group consisted of children showing definite archicapillaries as described by Jaensch, comprising 17 per cent of all the feebleminded children. (2) This group included 53.4 per cent of the feebleminded children. They showed deviations from the normal which do not correspond to any of the types described by Jaensch—broadening of the loops, widening of the capillaries themselves, and a pathologic uniformity and simplicity of the shape of the capillaries. (3) This group, consisting of 29.6 per cent, represented the children with capillaries as near the normal type as were found in the institution. Even in them, however, there were slight deviations from the normal. A comparison of all of these with the pictures of the normal children, shows that the capillaries of practically all the feebleminded were different from those of the normal children.

The author comes to the conclusion that examination of the structure and shape of the capillaries is of value in diagnosing feeblemindedness. Furthermore, the type of pathologic process found, whether nearer to the primitive archicapillaries or to the normal type, is indicative of the degree of mental deficiency. It is an important guide in an attempt to train and teach the feebleminded child, and in cases in which the mental deficiency is associated with possible endocrine disturbances, close observation of the development of the capillaries under treatment is a useful guide and indicator of progress.

MALAMUD, Foxborough, Mass.

PSYCHOLOGIC INVESTIGATIONS OF THE EFFECT OF SEA CLIMATE ON CHILDREN. HEINRICH VOIGTS, Monatschr. f. Kinderh. **38**:225 (Jan.-Feb.) 1928.

By psychologic methods the author investigated the effect of sea bathing, sun baths, wind and air baths as well as the combination of sea and forest air.

There are so many variables depending on the season, temperature and direction of the wind that it is hard to form definite conclusions. In a general way, sea bathing and sea air seem to refresh the children physically, although the anemic nervous children were often relaxed. As a rule, the psychomotor irritability was increased, with diminution of the apperceptive function.

The happiest combination seemed to be that of forest and sea. The forest air quieted those children who were stimulated by the sea bathing and so, in the case of nervous children, offered an excellent means of controlling the treatment.

GERSTLEY, Chicago.

A Familial Disease with Special Involvement of the Basal Ganglia. L. Kalinowsky, Monatschr. f. Psychiat. u. Neurol. **64**:168 (Oct.) 1927.

Among the heredodegenerative diseases, types involving the basal ganglia are not common. They include Huntington's chorea, Westphal-Strümpell's disease, and Wilson's disease. In 1922 and 1923, a new entity was added to this group by Hallervorden and Spatz. They described two cases of almost pure degeneration of the pallidum and the pars reticularis of the substantia nigra. The author has had an opportunity to make a careful study of a family showing three similar cases.

There was no history of previous nervous disease in the family. There were four children — three sons who were all affected, and one daughter who escaped. The onset occurred at the age of 9 or 10 years, with pes cavus equinus and beginning spasticity of the legs. One or two years later, there was beginning impairment of vision and progressive dementia. The fully developed picture showed: an advanced dementia; a tendency to compulsory laughter; optic atrophy with marked but incomplete loss of vision; marked difficulty in speech —the speech being explosive and incapable of modulation; moderate rigidity of the arms without paresis; rigidity of the legs in adduction, with increased deep reflexes and inconstant Babinski sign; flexion of the knees; deformity of the feet — a combination of pes cavus, equinus and club foot; incontinence; normal potentia and increased libido. The whole picture is completed by extrapyramidal, hyperkinetic symptoms, differing somewhat in the three cases: (1) hyperkinesias of athetotic character in the head and hands; (2) tremor of the hands; (3) tremor of the hands and palilalia.

The oldest brother died at the age of 26 of bronchopneumonia. The brain showed, macroscopically, general narrowing of the convolutions as far back as the parietal lobe. Frontal sections showed a shrinking of the medullary substance. The striking thing, however, was a brownish discoloration of the globus pallidus and a brownish green discoloration of the substantia nigra. Microscopically, there were diffuse changes throughout the brain and distinctly focal changes in the globus pallidus and zone reticularis of the substantia nigra. The diffuse changes included some loss of cells with glia increase throughout the entire cortex, emphasized in the precentral gyrus. The temporal and occipital lobes were relatively intact. The cerebellum showed much reduction of Purkinje cells. The spinal cord showed some diffuse pallor in the pyramidal tracts, and in the columns of Goll and Burdach. The focal changes, involving the pallidum and zona reticulata of the substantia nigra, consisted of: a loss of cells, with much damage to those remaining; a more or less diffuse glia proliferation; the presence of curious rounded structures, described in their cases by Hallervorden and Spatz and wrongly classed by them as swollen axis cylinders, and the packing of the whole stroma with pigment masses and concretions, most of which contain iron and give to these structures their characteristic macroscopic appearance. In Weigert preparations the pallidum resembles Vogt's status dysmyelinatus.

The mesodermal tissue was not involved. There was no evidence of inflammation. The process was primarily a degenerative one, and that it was still active was evidenced by the presence of fat granule cells.

That one is dealing with a heredodegenerative disease is evidenced by: the familial character; the striking uniformity of the picture in all the reported cases; the finding of degenerative changes without evidence of inflammation. Clinically, the cases are characterized by progressive dementia, optic atrophy, and on the motor side by a combination of pyramidal and extrapyramidal symptoms. Pathologically, there is elective involvement of the pallidum and the zona reticulate of the substantia nigra. The existence of similar cases, as reported by Hallervorden and Spatz, suggests some connection between the two structures involved. Mirto demonstrated a phylogenetic connection; on the anatomic side, Spatz showed a small cell column joining them; a physiologic relationship is suggested by the similarity in their iron content.

Selling, Portland, Ore.

THE PATHOGENESIS OF MONGOLIAN IDIOCY IN THE LIGHT OF MONGOLISM OCCURRING IN TWINS. KNUD H. KRABBE, Acta Psychiat. et Neurol. **1**:337, 1926.

Mongolian idiocy is usually considered to be the result of some degenerative process affecting the child during fetal life. It has not been reported often as occurring in more than one member of a family, but there are a number of reports of cases in which one twin was a mongol and the other normal. Only three instances have been reported in which both twins suffered from mongolian idiocy. The author reports five examples of mongolism in twin children. In four instances, one twin was a mongol, the other, normal. In the fifth case both twins were mongols. The sex distribution was as follows: (1) female mongol, male normal; (2) female mongol, female normal; (3) male mongol, male normal; (4) male mongol, female normal; (5) female mongol, female mongol.

The fact that one child of twins may suffer from mongolian idiocy and the other be normal seems to indicate that the mongolism is not due to action of any toxic influence on the child in utero. In two of the five instances cited by the author the twins must have been biovular because the sexes are different; it seems probable that in the other two instances in which one twin was normal, the children were the result of a biovular pregnancy although the sexes were the same. It is probable, therefore, that, in the case of the mongolian twins reported, the children resulted from a monovular pregnancy because the sex is the same.

It has been found almost constantly that children suffering from mongolian idiocy are born of mothers who are advanced in years. The author concludes that some degenerative process, possibly the result of age, affects an ovum that develops into a mongolian child, and that the condition is determined by the state of the ovum before impregnation.

PEARSON, Philadelphia.

GENERAL PRINCIPLES, TECHNIC AND RESULTS OF NEW TREATMENT OF INFANTILE PARALYSIS. H. BORDIER, Acta Psychiat. et Neurol. **2**:1, 1927.

The method described in this article consists in the association of radiotherapy of the spinal cord and of diathermy of the parts involved with such electrotherapy of the atrophied muscles as may seem necessary. The combination is based on the fact that the lesion consists early of a diffuse meningomyelitis with edema, followed by the destructive action on the anterior horn cells. In a total of sixty-five patients treated, the results were complete recovery in more than 15 per cent and amelioration in 75 per cent.

CONGENITAL HEREDITARY ONYCHOGRYPOSIS, TOTAL ALOPECIA, AND SCHIZOPHRENIA. MAX SCHMIDT, Acta Psychiat. et Neurol. **2**:317, 1927.

An extremely interesting family group is described, of which two members constitute the immediate material. These are sisters presenting a pronounced leptic bodily structure; with onychogryposis of all fingers, generalized alopecia, and mental symptoms indicative of dementia praecox. A chart traces the heredity back to the great grandparents of the patients; one of these ancestors (male) had onychogryposis. The F generation had four members, of whom three were definitely affected; the F_2 generation had ten; in the F_3 generation (that of the patients) there were seventeen of forty-two who were known to have onychogryposis. The literature is reviewed, and the article includes a discussion of the possible related condition of "blue sclerotics."

ANDERSON, Philadelphia.

THE CORTICAL CENTERS IN RELATION TO THE SENSE OF TASTE AND SMELL. F. HERZOG, Orvosi hetil. **71**:1488, 1927.

The author reports his observations on thirty-three patients with tumors. Paralysis of the sense of smell and taste was found in ten patients, four of whom

showed paralysis of the sense of smell, five of taste and one of both senses. The disturbances can be explained by changes of internal secretion, and it is difficult to explain it as a general symptom of the tumor. Disturbance of smell seems to be a focal symptom of the hippocampus. In one patient there were signs of excitation in the center of smell associated with paralysis of taste. This seems to prove that the cortical centers of smell and taste are close together, particularly in this case. All general symptoms or other focal symptoms were absent.

ZENTAY, St. Louis.

COLLOIDAL REACTIONS IN THE CEREBROSPINAL FLUID IN VARIOUS DISEASES OF CHILDREN. L. TSCHERNYSHKOVA, J. Pediat. (Russian) **2**:223, 1927.

The subject of the author's studies was the Lange colloidal gold reaction, and the resina benzoe reaction (Guillain, Laroche, Lechelle).

The literature concerning the colloidal reactions and their significance in the clinic is mostly concerned with syphilitic diseases of the central nervous system. It is extensive and is of great importance for the diagnosis of neurosyphilis. The author's problem was to verify on her own material the somewhat scant data of different authors concerning nonsyphilitic organic diseases of the central nervous system; to verify the data for the functional diseases of the central nervous system; to analyze the changes in the spinal fluid in different metabolic diseases, especially those affecting the endocrine glands; to analyze the influence of different toxic processes on the physicochemical changes in the spinal fluid in the pathologic disorders of nourishment in infants. The author examined 215 spinal fluids. In the first group of organic diseases were included mostly meningitis: tuberculous, epidemic, purulent; encephalitis, polymyelitis, hemorrhages in the cerebral cavity, jacksonian epilepsy, and other diseases, such as tumor of the brain, rabies and idiotism of syphilitic character.

Conclusions.—1. The reaction with the Lange test, as is the case with all colloidal reactions, is not specific for the diagnosis of syphilis, because nonspecific bodies take part in the reaction.

2. The types of curves in different diseases in the colloidal gold reaction and other colloidal reactions depend on the qualitative difference of the colloidal content in the spinal fluid and cannot be strictly differentiated, as was done when the method was first applied. These curves give only the possibility of differentiating an organic disease of the central nervous system from an inorganic one, and if the colloidal gold reaction and the benzoe reaction are used, it is possible to differentiate processes of degenerative character affecting the vascular system of the central nervous system and processes of evolutionary character involving the meninges.

3. Colloidal reactions, while not specific for syphilis, enlarge the diagnostics of the diseases of the cerebrospinal fluid. The reactions are always positive with organic changes of the central nervous system and the meninges, no matter what the origin of the disease may be. Their value is in the fact that one can always draw a definite limit between the disease of the brain and diseases without any anatomic changes in the brain, but with nervous symptoms of functional or toxic character, as spasmophilia, uremia, meningism, in acute infections and other diseases.

4. The colloidal reactions are particularly valuable in organic diseases of the central nervous system of nonsyphilitic character. If the process passes without acute manifestations and therefore without any increase in albumin, pleocytosis or globulin reaction, colloidal reactions are the only basis for a correct diagnosis. In cases of syphilitic character the colloidal reactions are less valuable, because the diagnosis in such cases could be made by the Wassermann test.

5. The colloidal reactions give a picture of the qualitative interrelations of the colloids of the spinal fluid, which were not known before and which give the possibility of penetrating more thoroughly into the biochemical nature of the pathologic process.

SEVERAC, Philadelphia.

Diseases of the Eye

CASE OF CEREBRO-MACULAR DEGENERATION. F. J. POYNTON, Proc. Roy. Soc. Med. **21**:226 (Dec.) 1927.

A boy, aged 6 years, had always been backward. His sight began to fail in May, 1926, and vision was completely lost shortly after that time. The patient had measles early in 1926. Physical examination showed that he was completely blind; speech was mumbling and indistinct. Bilateral optic atrophy and extensive scarring at each macula were present. The knee jerks were absent. The Wassermann reaction was negative. The loss of sight was first noticed after an attack of measles, and the question arises whether there was any relation between the measles and the onset of the change in the eyes.

WILLIAMSON, New Orleans.

Diseases of the Ear, Nose and Throat

PHYSICAL CAUSES OF DEAFNESS; REPORT OF COMMITTEE, DIVISION OF MEDICAL SCIENCES, NATIONAL RESEARCH COUNCIL. C. W. RICHARDSON, G. E. SHAMBAUGH ET AL., Arch. Otolaryng. **7**:415 (May) 1928.

A survey of present conditions and methods of schools for the deaf in the United States was made. The schools were grouped into five units centering about New York City, Chicago and Philadelphia. Examiners were appointed and uniform examinations and records made. The work covered the case history, physical examination and a limited amount of laboratory tests. In all, 3,734 children from 19 schools and institutions were examined. Several months were required for this and several more for classifying and organizing the data found.

It was found that there is practically no difference of incidence between the two sexes in either congenital or acquired deafness. More than 59 per cent of acquired deafness began before 3 years of age. This probably was partly due to the fact that many cases of acquired deafness were really congenital deafness that had not been recognized as such in the infant. The percentage of incidence decreases as the age increases. The earlier years of life are those in which the acute infectious diseases, often the cause of deafness from toxic neuritis of the eighth nerve, are more likely to be found. Meningitis was shown to be responsible for 209 cases; scarlet fever for 100; measles, 97; influenza, 91; infantile paralysis, 37; suppurative otitis media, 66; whooping cough; 42; probable syphilis, 24 and fracture of the skull, 24. Many of these groups are subdivided into degrees of deafness and their relation to the varying degrees of vestibular involvement accompanying the deafness. In forty-seven of the cases caused by scarlet fever the patients were free from otitis media. Toxic neuritis resulting from the infectious disease is the probable cause of the deafness in this group.

Special mention is made relative to tonsils and adenoids. In 1,562 of the children, tonsils were in situ; in 1,224, successful removal of the tonsils and adenoids had been accomplished. Of the latter group, 482 showed evidence of lesions of the middle ear, and 742 were free from such evidence. In the former group (tonsils in situ), 622 had trouble with the middle ear and 940 did not. The conclusion is made that although mild deafness is common with acute inflammations of these lymphoidal structures due to tubotympanic catarrh, the more severe types are little affected by such inflammatory conditions.

Of the total number examined, 723 were found in whom heredity and consanguinity appeared to be etiologic factors; of these, 81 more cases of partial than total deafness were found. The cases of ten pairs of twins who were deaf were recorded. Vestibular responses were present in about 5 to 1 of this group.

Of the persons with acquired deafness, 80 per cent did not show a record of otitis media as an etiologic factor and of the remaining 20 per cent certainly some did not have otitis media severe enough to cause a deafness sufficient to require institutional care.

Forty-seven per cent of all examined were totally deaf; the remaining 53 per cent showed varying degrees of hearing. In about 60 per cent of those totally deaf, the deafness was congenital.

The Schwabach test showed an absence of bone conduction in 2,040, present but shortened in 795, normal in 94 and prolonged in 50. Of the 2,040 without bone conduction, 1,556 showed remnants of hearing by the audiometer; of the 795 with shortened bone conduction 736 gave positive audiometer tests. Marked defects in speech were present in about one half of those with some hearing. About one third of those deaf to the voice were also deaf to the audiometer.

In general, patients with congenital deafness were less likely to show vestibular disturbances than those with acquired deafness, especially when there had not been a toxic neuritis of the eighth nerve or an otitis media involving the whole labyrinth. Interesting statistics are given showing the relationship of the various vestibular tests to the different classifications of deafness.

MASTOID PUNCTURES IN INFANTS. ISADORE FREISNER and SAMUEL ROSEN, Arch. Otolaryng. **7**:524 (May) 1928.

A method for puncturing the mastoid antrum in infants for purposes of diagnosis and treatment is described. It had been done thirty times on living infants with innocuous results as well as thirty-two times post mortem.

BARNETT, Chicago.

THE RAPID DEATH IN INFANTS OPERATED ON FOR MASTOIDITIS WITH A DISCUSSION OF THE OPERATIVE TECHNIC AND RESULTS. GEORGES CANUYT, Rev. franç. de Pediat. **4**:101, 1928.

Because of the frequently fatal results following operations on the mastoid in infants, the author has changed his technic from an extensive operation under a general anesthetic to a simple opening up of the part without curettage under a local anesthetic, ethyl chloride. Since 1924, with the new technic, not any fatalities have occurred. Twenty-seven infants have been operated on.

LESLIE, Evanston.

Diseases of the Skin

PROGERIA. ROBERT HUTCHISON, Proc. Roy. Soc. Med. **21**:227 (Dec.) 1927.

A boy, aged 4 years, showed the following on examination: The scalp moved a little on the skull, and the hair was fine and scanty. The skin of the whole body was dry. The four erupted teeth were malformed. Two unerupted teeth could be seen. Some cervical adenitis was present. The Wassermann reaction was negative. A section of a piece of the skin showed neither sweat glands nor ductus. The case differed from the classic examples of progeria, but it seemed to the author nearer to that than to any other condition.

WILLIAMSON, New Orleans.

CYTOSTEATONECROSIS OF THE SUBCUTANEOUS TISSUE IN THE NEW-BORN. P. WORINGER and G. WEINER, Rev. franç. de pediat. **4**:57, 1928.

The authors discuss a syndrome occurring in the new-born characterized by the appearance of areas of induration in the skin and subcutaneous tissue, which last over a period of several weeks and disappear spontaneously. The condition has been described under the names of scleroderma, scleremia, or a curable induration of the skin. The authors object to the foregoing terms and point out, confirming their statements by histologic evidence, that the condition is one of cytosteatonecrosis of the adipose elements in subcutaneous tissue and corresponds in all

points to the traumatic cytosteatonecrosis of the adult. The lesion is characterized by the saponification of the fat contained in the adipose cells, which acts as an irritative foreign substance producing inflammation and later, resorption. Obstetric trauma is said to be the cause of the condition.

LESLIE, Evanston.

Surgery and Orthopedics

SURGICAL COMPLICATIONS OF TYPHOID FEVER IN A CHILD. CHARLES K. P. HENRY, Canad. M. A. J. **18**:174, 1926.

The author presents the record of a case of staphylococcic infection of the hip joint occurring in a child, aged 4 years, who had typhoid fever.

SURGICAL TUBERCULOSIS IN CHILDREN. D. K. MEEKISON, Canad. M. A. J. **18**:180, 1928.

The author presents in detail his study of 100 cases of surgical tuberculosis in children. He concludes that tuberculosis of a joint or gland or Pott's disease does not exist per se, but is a manifestation of a general disease. Detailed tables of the results of his investigation are presented. In this series of 100 cases, tubercle bacilli were recovered from the urine in 11.8 per cent. They were shown to be present in the upper respiratory tract in 11.1 per cent. Routine examinations of the chest revealed the fact that two thirds of the patients showed foci in the lungs.

MOORE, Omaha.

Miscellaneous

DISCERNMENT OF HUMAN RACES BY BLOOD, PARTICULARLY OF RUSSIANS FROM JEWS. E. O. MANOILOFF, Am. J. Phys. Anthrop. **10**:11, 1927.

Blood tests of 880 Jews and 1,120 Russians, by the author's new method, have led to the following results: The determination of different races by blood with author's reagents—in this case to distinguish Jewish blood from Russian—gave the correct result in 91.7 per cent of the cases tested. The oxidizing process was produced in Jewish blood more quickly than in Russian. The reaction may be of value in medicolegal investigations. In mixed marriages the reaction gives indications of the influence exercised on one race by another.

AUTHOR'S ABSTRACT.

MANOILOFF'S "RACE" REACTION AND ITS APPLICATION TO THE DETERMINATION OF PATERNITY. ANNA T. POLIAKOWA, Am. J. Phys. Anthrop. **10**:23, 1927.

The results of the author's blood tests on more than 1,500 persons, according to the Manoiloff method, show important corroboration of the claims of this author. The tentative conclusions are that: In racially pure marriages the child's blood has the same reaction as the father's and the mother's. If the child's and the mother's blood give a different reaction, the father does not belong to the mother's nationality. If the child has a distinct race reaction which does not correspond to the mother's nationality, the father may belong to the nationality the reaction of which has been found in the child. Attention is also called to anthropometric and other methods of the identification of parentage.

ALEŠ HRDLIČKA.

VENTILATION IN THE HOME. U. S. P. H. S., April 9, 1928.

In a five-year study that the United States Public Health Service has recently completed, it was found that diseases of the lungs (respiratory diseases) accounted for nearly half (47 per cent) of all the cases of sickness reported. Ventilation has been the subject of much research. It has been

found that the most comfortable temperature as well as the most healthful one is between 68 and 70. There should be a slight amount of air motion in all rooms such as is produced by a small opening in a window. If the air is kept at this temperature, the moisture of air or humidity will be kept at a satisfactory, healthy point. Studies have been made in schools in which the rooms were kept at 68.5 and 66.5. They showed that there was 70 per cent more colds among the pupils in the rooms with a higher temperature than among those in the rooms in which the temperature was maintained at 66.5.

SANFORD, Chicago.

PROCEEDINGS OF THE GERMAN PEDIATRIC SOCIETY, 1927. Monatschr. f. Kinderh. **37**:289 (Dec.) 1927 and **38**:1 (Jan.-Feb.) 1928.

The thirty-eighth session of the German Pediatric Society was held in Budapest in September, 1927. The meeting opened with a tribute to the memory of Otto Heubner by the presiding officer, Johann von Bokay.

The scientific program was opened by H. Finkelstein, who reviewed the past work and brought forth additional clinical evidence in favor of the idea of alimentary fever. Following this, a number of papers were devoted to studies in metabolism. Rietchel did some work on salt fever, and Birk continued his studies on the metabolism of fever. Langstein read a review of the present status of infant feeding. The Finkelstein ideas are still generally accepted. A number of papers were devoted to contagious disease. Langer described an encephalitis due to chickenpox. Buschmann believes that the Calmette inoculations are of value in preventing tuberculosis. Opitz and again Nobel discussed tuberculosis bacteriologically and pathologically. Goebel reopened an old subject, bringing evidence of the activation of tuberculosis by measles.

Monrad presented interesting observations on pyloric stenosis. One boy who died from pneumonia, six months after medical cure of pyloric stenosis, showed much less muscular hypertrophy than another dying one month after cure. A third, dying one and one-half years after discharge, showed a normal pylorus.

In treating patients who have congenital syphilis, Heschéles found the malaria treatment to have some influence on the spinal fluid. Weiss described conjunctivitis as a sign of congenital syphilis. Spirochetes were present in the secretion from the conjunctiva.

Johan, studying scarlet fever, believes that the Dick prophylactic immunization is extremely valuable.

Leiner reported experiments in cultivating organisms from the fluid of cantharides blisters and also recovering organisms from eels which were laid on patients. The fluid of blisters in measles and chickenpox contains the causative organism. Typhoid organisms were also contained in the blister and typhoid, spirochetes and malaria plasmodia were found in the eels.

Spectroscopic examination of the blood in the study of avitaminosis was introduced by Kolath. Optochin was reintroduced in the treatment of persons with pneumococcus empyema.

Considerable time was given to discussing rickets. Gyorgy believes that the metabolic aspect has not been exhausted. Huldschinsky reports that the use of ultraviolet rays did not prevent the development of craniotabes in early infancy. Jundell defends his observations on the beneficial effects of underfeeding. A most promising and original field of study was offered by Fritz Demuth. Using the Carrell method of the growth of tissue in vitro, he has been able to keep cartilage cells alive and is studying the effect of various substances on their growth.

In studies of metabolism, Maurer casts some doubt on the idea that the thyroid is the sole control of iodine metabolism. Freudenberg studied a lipase found in breast milk and Scheer, a lipase in saliva. Papers by Schiff, Bessau, Mautner, Bosch and Nitsche discuss the interrelations of alimentary intoxication, water metabolism and acid and alkali balance.

The session must have been an excellent one. A great deal of original work was reported. The proceedings in the *Monatschrift* are for the most part abstracts of the papers, and the original contributions will appear in other periodicals and will probably be reviewed in more detail.

GERSTLEY, Chicago.

INTRAMUSCULAR INJECTIONS OF BLOOD IN DISEASES OF INFANCY. ANNA EBERT, Ztschr. f. Kinderh. **43**:625 (July) 1927.

More than half of the forty-five patients cited, those with chronic disturbances of nutrition complicated by pyelitis, furunculosis, otitis media, etc., ranging from severe to very severe forms, were treated favorably with intramuscular injections of human blood, without harmful results. There was not only a sharp change in the general condition for the better, but a marked gain in weight. In conjunction with other curative measures, this form of therapy seems to be one which should be used, and it deserves special consideration because it is practical. From 20 to 40 cc. of blood from the parents or from the physicians was given at intervals of from four to six days.

EMERSON, Boston.

THE INFANT MORTALITY IN BASEL FROM 1870-1925. RIVA WULFAHRT, Inaug. Diss., Basel, 1927.

In a critical study of infant mortality in Basel from 1870-1925, the author points out the particular factors which are responsible for the recent marked decrease in the infant death rate. From 1870-1907, there was a gradual fall in accordance with the decrease in the total mortality. Since that time the fall has been more abrupt and far greater than one would expect from the simultaneous decrease in the birth rate. From an analysis of the causes of death, the calendar month and the month of life in which the deaths occur, one sees that since 1907 there has been a marked decrease in the deaths from digestive disturbances, that with this the summer peak in infant mortality has entirely disappeared, and that the proportion of deaths during the first month of life has increased from one-third to one-half. Congenital debility, prematurity and injury at birth now take the greatest toll. Among the factors responsible for the change since 1907, the author emphasizes the systematic propaganda for breast feeding, the formation of societies for infant care with the nursery and milk kitchen and the establishment of welfare stations through private organizations under the supervision of the city board of health.

LESLIE, Evanston.

INHALATION OF EPINEPHRINE AND ITS EFFECTS. I. WEISS and G. MAGASSY, Orvosi hetil. **71**:1326, 1927.

Epinephrine can be given in the form of inhalations by the use of the proper apparatus. It stops asthmatic attacks promptly. Epinephrine introduced into the respiratory tract does not cause any increase of blood sugar or of blood pressure. This seems to prove that it is absorbed only in small quantities from the mucous membrane of the bronchi. Its effect seems to be in local action in the small bronchi.

ZENTAY, St. Louis.

DISEASE CONDITIONS OCCURRING IN PERSONS WHO HAVE ALMOST DROWNED. J. ED. STUMPFF, Nederl. Tijdschr. v. Geneesk. **72**:767, 1928.

Between 1915 and the end of 1927, more than 1,000 persons who had nearly drowned were transferred to the author's department in the Binnen-Gasthuis at Amsterdam; among them were many children. The author describes the conditions that may occur as a consequence of drowning; of all the patients, sixty-seven had a severe involvement of the lungs, but this was usually of a mild nature, so that at the end of the second or third day the patient had recovered. Next to

these slight cases came those in which a true aspiration pneumonia developed. In the author's opinion, the prognosis of this bronchopneumonia was also favorable. The third disease of the lungs found in these patients was lobar pneumonia. In typical cases, this disease began within twelve hours after the accident. The classic symptoms of the genuine inflammation of the lungs were present, though deviations from the typical course were not rare. The prognosis was bad. This was independent of the age of the patient, but in the author's opinion the cause of the disease must be here considered, namely, the influence of heart failure caused by the preceding suffocation and the bad condition of the whole organism (albuminuria, glycosuria), but principally the aspiration of the filthy water of the canals. The last named fact gave rise to simultaneous infections, in consequence of which pneumonia that resembled the dangerous pneumonia of the influenza epidemic appeared. The results of autopsy in many cases confirmed this.

Commonly, complications such as disease of the lungs begin in the first twenty-four hours; it is the custom to dismiss the patients who have a normal temperature for twenty-four hours and no complaints at the end of two days. It has been known for some time that occasionally, long after escape from drowning, diseases of unknown etiology may occur in the lungs and sometimes in the intestines. The discovery of *Spirochaeta icterohaemorrhagiae* has given an explanation of some of these cases. The author gives an example of a typical case of Weil's disease, in which the leptospirilis was found. In his older reports the author could find several cases in which the same diagnosis might have been made with great probability. The etiology of a more or less characteristic disease which occurs a longer time after submersion, especially in children, seems now also to be the same. Extreme exhaustion, enlarged spleen and recurrent fever are the principal symptoms in these children. Since it became known that icterus may be absent in 60 per cent of the patients with spirochetal infection, the author has investigated whether in the latter cases of late involvement in children a specific infection also had taken place. In one case, this opinion was confirmed.

In rare cases a severe general infection develops after submersion, of which fever, exhaustion and persistent diarrhea are the principal symptoms. In these cases an infection with Gärtner's bacillus could not be excluded until now, though its nature is not yet proved and the resemblance to the severe cases of spirochetal infection is great.

S. VAN CREVELD, Amsterdam.

THE SURPLUS OF BOYS IN STILL-BORN CHILDREN. J. SANDERS, Geneesk. Gids. **5**:1101 and 1129, 1927.

The well known fact that there are born more boys than girls has often been an object of study, especially in Holland during the last few years. In 1923, the Dutch statistician Methorst concluded that difference in age between the parents in itself does not have an influence on the surplus of boys. In 1926, Mysberg formulated the hypothesis, partly based on the experiments of MacDorell and Lord in America, that with conception the proportion between the sexes probably is 1:1, but that in the first two or three months more female embryos die; hence, the surplus of boys in the fourth and following months is large. In the later months of gravidity, however, more male embryos die, so that the surplus would become steadily smaller, to reach at last 105:100 in the living born. According to this hypothesis, the female embryo would have a smaller vitality. The larger percentage of boys in the still-born children has been explained by different authors to be caused by mechanical factors, i. e., by the fact that boys are larger than girls.

To control these and other conceptions, Sanders has made a statistical investigation of all new-born children who died in the large obstetric clinics of Holland between 1917 and 1924. He investigated the deaths of 3,420 new-born children registered as still-born. He divided his material according to sex, age of the fetus and, in a number of groups, to the cause of death. The material consisted of 1,807 full-term children (1,087 boys and 720 girls) and 1,613 pre-

mature children (837 boys and 776 girls). In the full-term children of all his groups he found a surplus of boys with the exception of one group (congenital abnormalities of the child). In this group he found, according to an already well known fact, that congenital abnormalities occur more frequently in girls than in boys. As regards the group classified according to the mechanical cause of death, the author found here the surplus of boys in full-term children to be 166.2 and in premature ones, 122.4.

On the basis of a statistical calculation of his results, the author comes to the following conclusions: The mechanical cause has a larger influence on the mortality of the full-term boys than on that of the full-term girls. This influence, however, is not so large as is generally supposed. The congenital abnormalities occur more frequently in girls than in boys. The number of male fetuses which die in consequence of intoxication is larger than that of female ones. According to the numbers of the children registered as still-born in Holland and the figures obtained from the clinics, it is the author's opinion that the surplus of boys in an earlier time of gravidity does not increase; this is contrary to the generally accepted opinion. The author concludes that, next to the mechanical factor, there exists definitely an important biologic cause for the surplus of boys in the still-born children.

S. VAN CREVELD, Amsterdam.

CONSTITUTIONAL KRETSCHMER TYPES AMONG SCHOOL CHILDREN. V. S. KRASSOUSKY, J. Pediat. (Russian) **2**:197, 1927.

The author thinks that the theory of Kretschmer on the classification of different types according to the constitution of body and character in adults can also be applied to school children. At present, there are two points of view on constitution. Some authors consider, as the basis of constitution, only genotypical characteristics, that is, constitution is regarded as the sum of gynotypical, physical and psychic, characteristics fixed at the moment of fecundation (Kretschmer, Mathes, Bauer and others). Some think that constitution is the sum of genotypical and paratypical characteristics. The latter are the result of different conditions of human life (Krehl, Kraus, Massloff and Krontovsky). The author's definition of constitution belongs to the second group.

The author examined 100 school children between 5 and 15 years of age. The problem was to discover whether the constitutional types of adults described by Kretschmer were to be found among school children, and the author's conclusions were as follows:

1. School children exhibit the same division into types according to the constitution of body and character as was found by Kretschmer in adults.

2. School girls do not have a less definite constitutional type of body and character than school boys.

3. According to Kretschmer, in 79 per cent of the cases the given constitutional type of body structure corresponds to the constitutional type of character, while in 21 per cent of the cases a correspondence does not exist. This was confirmed by the author's results.

4. In the deviation from the fundamental constitutional type of body structure, the same deviations in the type of character also are observed.

It is necessary to note that the determination of constitutional types in children is of great importance for the pediatrician and the teacher. If it is known to which constitutional type a child belongs and which peculiarities of character are genotypical, or fixed paratypically, the teacher and the pediatrician can more easily individualize their approach to the child.

SEVERAC, Philadelphia.

Society Transactions

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

J. W. Epstein, M.D., *in the Chair*

Eighth Quarterly Meeting, March 7, 1927

Presentation of Pathologic Material. Dr. H. S. Reichle.

Pulmonary Tuberculosis with Cavity.—Physical signs of a cavity were present. At necropsy, the lungs were injected in situ, and after removal several sections were made. I believe that the cavity was not a true pulmonary cavity, but a localized tuberculous empyema. There was an extensive involvement of the pleura at this point. The microscopic sections have not been finished, so the final interpretation cannot be made.

Intussusception.—A specimen was taken from a child dying of intussusception. The small intestine had entered the large intestine for only a short distance when gangrene occurred and a resulting general peritonitis. This would perhaps explain why the clinical course was atypical, and why an early diagnosis of enteritis was made.

Tuberculoma.—The brain presented showed two tuberculomas, one in the cerebral peduncle and one in the cerebellum. The position of these lesions explains satisfactorily the syndrome that was observed clinically. There were cranial nerve and cerebellar manifestations on one side and a spastic paralysis of the extremities on the other.

Parotid Abscess Following Mumps. Dr. S. A. Wahl.

In the patient, aged 20 months, fluctuation of the parotid gland was observed fifteen days after the initial swelling, which was eighteen days after exposure to mumps. When the gland was incised, a considerable amount of blood and some gas escaped. There is a disagreement in the literature as to whether suppuration of the parotid is ever a true complication of mumps, or whether the etiology is entirely distinct from this disease.

Meningitis After Mumps. Dr. S. A. Wahl.

The patient, aged 6 years, developed a headache and vomiting during an attack of mumps. The classical signs of meningitis were present, and the spinal fluid contained 270 cells. Convalescence was uneventful as it usually is in these cases.

Two Mongolian Idiots, One a Negro; Treated and Untreated Cretins. Dr. C. L. Ruggles.

These cases were demonstrated to show the typical signs of mongolism — one being in a negro child, which is rather unusual — and to contrast the picture of mongolism and cretinism. Occasionally, there is some difficulty in differentiating the two conditions.

Sclerema Neonatorum. Dr. W. C. D. Millhoff.

The infant was first observed at the age of 16 days, at which time nothing abnormal was noted. At 3 weeks of age, infiltration of the sucking pads of the cheek occurred, and a little later these infiltrations were found in the subcutaneous tissue of the arms and shoulders. On incision into these nodules, a small quantity of milky fluid was obtained. The histologic picture showed numerous fat crystals

surrounded by fibrous tissue and extensive deposits of calcium. The calcium was easily visible in the roentgenograms. The theory that seemed most plausible was that there had been some toxic influence which damaged the fat cells.

HEMIPLEGIA DURING PERTUSSIS. DR. J. E. MCCLELLAND.

The child, after a severe paroxysm of coughing, was found to have a hemiplegia. There were no convulsions. Ophthalmoscopic examination revealed a bilateral papilledema of 1 diopter. The spinal fluid was under increased pressure but did not contain cells or pigment. In the differential diagnosis, hemorrhage, encephalitis and abscess of the brain were considered. It has been found by several observers that papilledema sometimes occurs in uncomplicated cases of pertussis.

CONGENITAL SYPHILITIC OSTEITIS. DR. L. R. BRIGMAN.

An infant was first observed because of diarrhea. The Wassermann reaction was 4+, but at this time there were no symptoms of congenital syphilis. One month later, a painful swelling of the shoulder appeared. The roentgenogram showed typical changes, not only in the humerus of the painful side, but also on the opposite side. There was prompt improvement under antisyphilitic therapy.

LARGE THYMUS WITHOUT SYMPTOMS. DR. L. R. BRIGMAN.

The roentgenograms were taken because of a tumor in the neck. This did not reveal any abnormality in the neck except a large thymic shadow. There had never been any symptoms which might be associated with thymic enlargement.

A CASE OF REMITTENT FEVER WITH ANEMIA AND ENLARGEMENT OF THE LIVER AND SPLEEN. DR. C. T. J. DODGE.

A girl, aged 5 years, presented a rise in temperature to as high as 106 F. at a fairly uniform interval of from seventy-five to ninety hours. The peaks of temperature occurred between midnight and 3 a. m. The spleen and liver were markedly enlarged and the superficial lymph nodes were also enlarged. There had been no jaundice. The blood picture had shown only slight variations from the normal. Repeated blood cultures remained sterile. Tuberculin and Wassermann tests were negative. The results of repeated examinations for malaria parasites had been negative. Roentgenograms taken early in the course of the illness revealed a slight widening of the hilum shadow and no apparent pathologic process in the paranasal sinuses. A recent roentgenogram showed a definite opacity of one of the maxillary sinuses. The fever has occurred less frequently in the past week, and the patient shows definite improvement in her general condition. Several diseases have been considered, but I do not feel that a definite diagnosis has yet been made.

OTITIS MEDIA AND MASTOIDITIS WITH SYMPTOMS OF COLLAPSE. DR. W. B. TAGGART.

An infant, aged 7 months, gave a history of having diarrhea for a few days. Both membrana tympani were reddened. On the second day at the hospital, the infant suddenly collapsed. A right antrotomy was performed and pus obtained. Twenty-four hours later, signs of collapse again appeared, and a left antrotomy revealed pus. Transfusions, infusions and other supportive measures have been employed, and the patient has shown gradual improvement.

MASTOIDITIS IN A PREMATURE INFANT, POSSIBLY OF CONGENITAL ORIGIN. DR. W. B. TAGGART.

The patient, a 7 months premature infant, weighing 1,500 Gm., had fever from the day of birth. At 2 weeks of age, a bilateral paracentesis was performed, but the fever persisted. A right antrotomy was performed and pus obtained. On a concentrated feeding, the patient gained 1,700 Gm. in six weeks.

TWO INFANTS WITH MASTOIDITIS. DR. J. I. HARTMAN.

Lantern slides were shown illustrating the hospital courses of two infants admitted at about the age of 5 weeks with symptoms of fever and vomiting. Subsequently, symptoms of collapse developed which were relieved for a time in each case by bilateral paracenteses of the tympanic membranes; they recurred again and were relieved by antrotomy. The postoperative care of such patients was emphasized. In one case, infusions and transfusions were given, and the child made an uneventful recovery; in the other case, in addition to these procedures, subsequent paracenteses and a second antrotomy were necessary in order to maintain adequate drainage.

DISSEMINATED BRONCHIOGENIC TUBERCULOSIS SIMULATING THE MILIARY FORM. DR. H. S. REICHLE.

The infant was first observed at the age of 3 months. There were no physical signs. The roentgenogram showed a diffuse process evenly distributed throughout both lungs. The tuberculin test was positive. During the three months in the hospital, there has been only slight fever at times, and except for the failure to gain at a normal rate, practically no symptoms of the disease have been noted. The roentgenogram now shows a picture more like the bronchiogenic type than it did on admission.

CONGENITAL LEAD POISONING. DR. J. D. PILCHER.

James, aged 11 years, showed mental retardation and a decided intention tremor with active reflexes. The condition seems to have been congenital, and as his father is said to have suffered from lead poisoning, it is considered that the condition in the son may have been caused by the toxic action of lead on the father's spermatazoa.

ALLERGIC PULMONARY AND BRONCHIAL GLAND TUBERCULOSIS. DR. J. D. PILCHER.

Robert, aged 1 year, was presented as having a pulmonary infiltration the result of an allergic reaction. He had a strongly positive tuberculin reaction.

PULMONARY TUBERCULOSIS: TUBERCULOUS OSTEOMYELITIS OF RIGHT FIBULA AND RIB. DR. J. D. PILCHER.

Leonard, aged 15 months, has been in the hospital eight months. On admission he had sinuses discharging from the lower right fibula and eighth rib on the right side; the liver extended to the umbilicus and the spleen was much enlarged; there was also pulmonary infiltration; the tuberculin test gave a strongly positive reaction. His general condition is now excellent; he had gained 7½ pounds (3.45 Kg.) the liver and spleen are much smaller; the processes in the bone are nearly healed, but the pulmonary infiltration persists. The processes are considered to be tuberculous.

A CASE OF PENTOSURIA. DR. H. J. GERSTENBERGER.

The patient, aged 14 months, was brought to the hospital because he was underweight and was not eating. In the routine examination, it was found that the urine contained a large amount of a reducing substance. Further study revealed that the blood sugar level was normal, being 107 mg. per hundred cubic centimeters. Tolerance tests did not change the results, and the history was negative as far as the administration of drugs that might reduce copper solutions is concerned. The reducing substance was found to be nonfermenting. It was therefore suggested that the substance causing the reduction in this child might be a pentose. This was established definitely by using Bial's test and the furfural reaction. It is interesting to note that the grandmother of the child is suffering from the same

condition. The father said that the grandmother had diabetes and that she was not taking insulin, but was simply somewhat careful of her diet. Naturally, this fact was of interest, and specimens of urine were sent for study. It was found that the reducing substance in the urine of the grandmother likewise was a pentose. The prognosis is good, and the cause of the condition unknown.

A Case of Aerophagia with Vomiting. Dr. H. J. Gerstenberger.

A poorly nourished infant, aged 1 month, had been subject to projectile vomiting of both water and milk at intervals. At the age of 3 weeks, breast milk was replaced with Eagle brand milk, but the vomiting did not change. Stools were passed once daily, but they were small and dark green; the infant lost in weight, weighing 500 Gm. less on admission than he did at birth. On admission, in addition to the foregoing symptoms, it was found that he was hypertonic, irritable and nervous, and a gastric-peristaltic wave was seen. At times he seemed to be in a tremendous state of tension, as if he were expecting something serious to happen. His fists were clenched, his arms were flexed, his knees were thrown up and his eyes were wide open, and he was staring. For some reason, I had the impression that this child had the habit of swallowing air. A roentgenogram showed the stomach to be markedly distended. Past experience has time and again taught me that a low fat, high sweet protein mixture such as boiled skimmed milk is of value in these cases. We therefore fed the infant double strength boiled skimmed milk with 6 per cent carbohydrate by tube and also gave him 1/500 grain (0.13 mg.) of atropine, hypodermically twenty minutes before each gavage. The improvement in every way was decided, and it was especially evident in the general attitude of the child. Instead of being nervous, awake and in tension, he slept and appeared phlegmatic. The vomiting quickly became less, and he gained weight tremendously, making a total gain of 1,400 Gm. in four weeks. This infant might well have been presented as having a case of pyloric spasm, and surgical intervention undoubtedly would have been resorted to by some physicians. The results obtained, I believe, indicate that the diagnostic conclusions and therapeutic course were justified.

A Case of Vomiting with High Fever, Marked Tetany and Severe Collapse. Dr. H. J. Gerstenberger.

The patient, aged 3 months, weighed 4,000 Gm. At birth, the weight was 8¾ pounds (3,968 Gm.). The child has received nothing but breast milk. Two days after birth, the infant began to vomit after some of the feedings, and has always been constipated. During the past few days, the vomiting has been worse and persistent. A stool, however, was passed on the morning of admission to the hospital. According to the record, on admission the infant had the appearance of being seriously ill. She was stuporous, in a state of dehydration, with sunken eyes and inelastic skin. A peculiar jerking was noticed, especially in the upper left abdominal areas. The jerkings seemed synchronous with the beat of the heart. Large, rapidly moving peristaltic waves were visible, running across the abdomen from left to right. The jerking just referred to was so marked that it was thought that perhaps a diaphragmatic hernia was present in this infant. Examination by roentgen ray, however, showed that the diaphragm was normal. No explanation has been given for the peculiar factor observed. A spinal puncture was performed, and the fluid was found to be normal. The facial phenomenon was positive, and the cathode opening contraction was obtained with 1 milliampere; in other words, spasmophilia was present. This was substantiated by the blood calcium and phosphorus determinations, the former level being 8.3 and the latter 11.7; in other words there was an enormous increase in the phosphate level of the blood serum. The hemoglobin was found to be 85 per cent, and the white cells numbered 22,000. The urine contained a small amount of albumin, a few casts, but no pus and no reducing substance. The blood sugar level was 117 mg. per hundred cubic centimeters. The temperature on admission was 41 C. (105.8 F.). On the

morning after admission, when most of the data just referred to had been obtained, it was appreciated that as a result of persistent mild and recent severe vomiting, the infant had an alkalosis followed by an active spasmophilic symptom-complex enhanced in its appearance by the hyperpyrexia and hyperventilation. It would seem from the examination of the blood that the increase in phosphate might be a compensatory phenomenon. On the basis of the data obtained, the child was fed boiled hydrochloric acid skimmed milk according to Scheer, and Ringer's solution was given subcutaneously and by mouth. Within twenty-four hours, the improvement was decided, and in forty-eight hours, the cathodal opening contraction was obtained with only 8 milliamperes, and the temperature had reached the normal level. At this time, the hydrochloric acid was removed from the food, and plain boiled skimmed milk with 6 per cent carbohydrate was given by gavage as previously.

The high white cell count would indicate that an infection was present and possibly responsible for the fever and for a secondary hyperventilation and a consequent active spasmophilia. However, no definite infection was clearly recognizable, and one therefore must assume that this entire picture, including the fever, was due to the changes in the physical chemistry of this infant's body as the result of the insidious and persistent vomiting which had begun so soon after birth. At present, the child is continuing its recovery and presents a picture which makes one believe it hardly possible that the child could have been as severely ill as described.

OPPENHEIM'S MYOTONIA. DR. H. J. GERSTENBERGER.

The patient, aged 16 months presented an extremely severe reduction in muscle tone of all of the muscles except the diaphragm. This was demonstrated by the teeter-totter movement of the thorax which is due to the lessening in the action of the intercostals and the continuing performance of the diaphragm. Another child in this family presented the same disease and died at the age of 4½ years with capillary bronchitis. The extreme degree of the condition in the patient makes the prognosis bad. The probabilities are that the child will succumb just as its brother did.

CONGENITAL SYPHILIS WITH PECULIAR RASH OR DERMATITIS ON THE NECK AND ON THE BUTTOCKS. DR. H. J. GERSTENBERGER.

A mulatto infant, aged 4 months, was presented because of the interesting observation made on a peculiar rash which was present when the child was admitted to the hospital. This rash was pustular, and the pustules were large (at least the size of a match head), high and well filled. Some of them were slightly umbilicated and resembled the cutaneous lesions of a vaccinia. The rash was intensive, but was limited to the region of the buttocks and the neck; in other words, to the areas that in infants are more often than others subjected to moisture. The facial expression of the infant was suggestive of syphilis. However, no dependable clinical signs of this disease were present. Dr. H. N. Cole, who saw the child, called the condition a pustular dermatitis, and suggested that it might have a syphilitic basis. The Wassermann test was 4+. However, before any antisyphilitic therapy could be started, the lesions disappeared, leaving a reddened base. In other words, this cutaneous lesion was not syphilitic and probably was improved by the better general and dietetic care given the infant in the hospital than in the home. The point that I wish to make is that had antisyphilitic therapy been started immediately, the conclusion probably would have been that the rash was syphilitic.

PARASINUSITIS WITH HYPERREGENERATIVE ANEMIA. DR. N. C. WETZEL.

The patient presented a moderately severe anemia. The hemoglobin was 30 per cent (Sahli); the red blood cells, 3,300,000, and the white blood cells 9,000, secondary to a fulminating parasinusitis which was in its most acute stage about

two months before presentation. Repeated hematologic and serologic studies had shown clearly that the condition was an anemia in which both elementary phases of normal cellular and pigment metabolism are greatly accelerated, red cell and pigment destruction, however, having prevailed, though not entirely so, over an especially pronounced degre of regeneration. That we are justified in this interpretation is distinctly shown by the presence of a moderate icterus of the plasma (Meulengracht's icteric index of 9) and the constantly demonstrable reticulocytosis of 24 per cent. We have, therefore, not found it logical to prescribe liver in this patient's diet, and we are attempting, on the other hand, to eliminate the absorption of hemotoxic products by daily nasal irrigations with 10 per cent dextrose solutions and occasional irrigations of the antrums of Highmore.

THROMBOSIS OF THE SPLENIC VEINS. DR. N. C. WETZEL.

A negro boy, aged 6 years, has now been with us about seven months, having also originally entered the hospital with the complaint of anemia. He did have a moderately severe regenerative anemia with splenomegaly, showing on the average a hemoglobin content of 35 to 40 per cent (Sahli), from 3,000,000 to 3,500,000 red blood cells and from 7,000 to 10,000 leukocytes, the icteric index of the plasma varying from 7 to 12 by Meulengracht's standard. While originally, a diagnosis of Banti's disease in the first stage was favored, it subsequently developed that the spleen would become small and even impalpable but a few days after it had extended from two to three fingerbreadths below the costal margin, then it would enlarge once more to its former size within a period of ten days or two weeks. Four such complete cycles have now been observed, and associated with this periodic change in the size of the spleen has been the discovery and identification of small to moderate amounts of occult blood in the stools coincident with the regression and contraction of the spleen. We have, therefore, concluded that this splenomegaly cannot be attributed primarily to hyperplasia of the parenchymatous elements, and further that such an enlargement, followed as it has been by complete and relatively rapid disappearance of the organ, could hardly be compatible either with fibrous interstitial overgrowth or with even a moderate degree of perisplenitis. Vascular factors must, accordingly, play the most important rôle in this recurring splenomegaly, and of these we believe a thrombosis of the splenic veins to be the most probable.

It is of passing interest to add that the daily administration of 90 Gm. of liver for a period of eighty days has influenced neither the degree of the anemia nor the cyclical character of the symptoms described.

NEW YORK ACADEMY OF MEDICINE SECTION ON PEDIATRICS

Regular Meeting, March 8, 1928

WILLIAM ROPES MAY, M.D., *Chairman, Presiding*

THE SEX FACTOR IN INFANT MORTALITY. DR. HARRY BAKWIN. (From the Department of Diseases of Children, College of Physicians and Surgeons, Columbia University and the Children's Medical Division and Department of Pathology, Bellevue Hospital.)

Sex is an important factor in determining the outcome of disease during infancy. During the ten year period from 1915 to 1924 inclusive, there were from 130 to 134 deaths in white male infants less than 1 year of age from all causes to 100 deaths in white female infants less than 1 year, in the United States Birth Registration Area. Since the proportion of males to females at birth during that period was approximately 106 to 100, it is apparent that

the death rate in boys is considerably higher than that of girls during the first year of life. This hypersusceptibility on the part of the male is evident before birth. Schultz found marked variations in the sex ratio of still births from month to month. During the third and fourth months of gestation, the ratio is high (121 to 117.5). In the fifth to the seventh months, it declines markedly (101.9), rising again in the eighth to the tenth months to a much higher figure than during any previous period (165 males to 100 females).

Variations in the Mortality Sex Ratio During the First Year of Life.—At birth the sex ratio is high (140). It rises markedly on the third day (to 147), after which it falls gradually until the third week. It then rises again, reaching another peak during the second month of life after which it declines gradually.

The Mortality Sex Ratio and the Death Rate.—It has been found that as the infant mortality rate falls, the sex ratio rises. In such countries as Sweden, England and Wales, in which mortality records have been kept for a great many years, the fall in the death rate has been accompanied by a rise in the sex ratio. Most other countries also show this increase in the sex ratio as the infant death rate has declined. Thus in the decade from 1841 to 1850, the infant death rate for England and Wales was 153 and the mortality sex ratio 122. Coincident with the fall in the death rate starting after 1900, the ratio began to rise, so that in 1926 with a death rate of 70 the sex ratio was 130. The ratio has risen not only for infants less than 1 year of age, but for all age subdivisions under 1 year and for children during the first five years of life.

ENVIRONMENTAL FACTORS INFLUENCING THE MORTALITY SEX RATIO

Regional Differences in the Mortality Sex Ratio.—For the same death rate the mortality sex ratio in different countries varies. The ratio is high in England, Wales and Scotland and low in Italy, Jamaica, Japan and Spain.

The Mortality Sex Ratio for Urban and Rural Communities.—The infant mortality rates are regularly higher in the United States for urban than for rural communities. Though the death rate is higher, the sex ratio, contrary to what one might expect, is also higher. Urban life is apparently not only less favorable for both sexes, but is particularly unfavorable for the male.

Seasonal Variations in the Mortality Sex Ratio.—The mortality sex ratio for infants less than 1 year of age is high during the winter and low during the summer months. This is true for diseases with a high winter death rate, e, g., pneumonia, as well as for those with a high summer death rate, as, e. g., diarrheal diseases. For infants during the first month of life the curve is reversed, the mortality sex ratio being higher during the summer months, but after the second month of life the mortality sex ratio for infants less than 1 year is regularly high during the winter and low during the summer.

It is suggested that the climatic, regional and seasonal variations in the mortality sex ratio during infancy are dependent on the different quantities of sunlight which reach the infant. England, Wales and Scotland are notoriously poor in sunlight, while Italy, Jamaica, Japan and Spain are countries which abound in sunlight and which have populations that live to a large extent outdoors. It seems reasonable to suppose that infants in rural communities get more sunlight than do those in the city where life is to a much larger extent confined to indoor living, and where sunlight, particularly the ultraviolet portion, is absorbed by dust and smoke. That the quantity of sunlight reaching the infant during the summer months is greater than during the winter months is obvious.

Some of the harmful factors of the absence of sunlight for infants are now well known. Ultraviolet radiant energy or a substitute is of the greatest importance in regulating calcium metabolism; it is necessary for the proper deposition of calcium in bone and for the maintenance of a normal calcium concentration in the circulating fluids.

It has been found that the calcium regulatory mechanism in males is much less stable than in females. In a series of 168 patients infantile tetany occurred more than twice as often in boys as in girls. Whether or not rickets is more common in boys than in girls has not yet been determined.

It seems reasonable to assume that the season of the year at which the sex ratio is lowest represents that regional climatic environment most favorable for the male. If the mortality sex ratio during the entire year could be reduced to its lowest seasonal level, many deaths would be prevented. During the five year period studied for the preparation of the chart on seasonal variations (1918-1922) there were 645,903 deaths from all causes in infants in the United States Birth Registration Area with a sex ratio of 133.8. If this ratio had been 126.5 instead, the lowest point reached by the ratio for that period, the lives of approximately 21,000 males would have been saved. This calculation is only for the birth registration area of the United States which constituted 53 per cent of the population in 1918 and 72 per cent in 1922.

It is therefore of more than academic interest to know what the environmental factor or factors are which react so unfavorably on male infants. If the hypothesis suggested proves to be true, namely, that variations in the amounts of sunlight through the stabilizing effect on the calcium regulatory mechanism determine the regional and seasonal differences in the mortality sex ratio, then a method for the reduction of the mortality sex ratio by means of artificial sunlight or a substitute is strongly indicated.

DISCUSSION

DR. ALFRED F. HESS: This is a difficult paper to discuss. I had no idea that the sex ratio was such a marked and constant phenomenon in infant mortality. One thing that makes the question difficult is that one has to attempt to eliminate all other factors. The fact that the same sex ratio obtains in utero indicates that it must have a deep and significant biologic basis. In that place and at that time of life one cannot think of lack of light as a factor, for it is known that congenital rickets does not develop. I do not think that one can be sure that sunlight plays the predominant rôle in this sex ratio.

In regard to the regional occurrence of the ratio, it is questionable to consider the mortality of a country, such as Italy or Japan, as a unit and compare it to that of another. Different parts of these countries have different climates. The northern part of Italy has a climate similar to that of New York City, whereas the southern part, about Naples, is mild and warm. A similar distinction holds true for the northern and southern parts of Japan. I wonder if there are any figures on the serum calcium in England and Scotland compared to those of some of the southern countries.

The most significant factor of this sex ratio is the remarkable reversal of the ratio in cases of whooping cough. Any one who finds out the cause of this phenomenon will discover an etiologic factor of this disease. It seems to me it must be of an endocrine nature, probably related to the sexual glands, although not necessarily the gonads. If the high mortality of males, in other words the typical sex ratio, is due to lack of sunlight, physicians might combat this mortality by subjecting infants to sunlight or artificial irradiation or by giving them foods exposed to ultraviolet radiations. If the irradiated foods or sterols were given more widely, it might affect the incidence not only of rickets but of other diseases as well.

DR. BAKWIN: It was not my intention to deny that the male is more susceptible than the female. The innate hypersusceptibility of the male, however, may be influenced by environment. Though the climate in various portions of Italy and Japan varies, on the whole infants in Italy and Japan receive more sunlight than infants in England, Wales and Scotland.

It has not been our experience that the serum calcium in infants is particularly stable. It varies with the season, being higher in the summer and lower in the winter. It also fluctuates in the course of infections, particularly pneumonia.

CONGENITAL INTESTINAL OBSTRUCTION. DR. RICHARD W. BOLLING.

The diagnosis of congenital intestinal obstruction may be made promptly and certainly in the majority of cases, and in a considerable proportion of these cases the anatomic conditions afford a promising field for surgical endeavor.

This paper concerned stenosis and atresia of the intestinal tract and volvulus secondary to abnormal intestinal rotation, excluding congenital stenosis of the pylorus and malformation of the anus and rectum, as well as those cases of chronic intestinal obstruction due to anomalies in rotation manifested later in infancy and early childhood. The author's personal experience comprises fourteen cases, one of abnormal rotation with volvulus and thirteen of intestinal occlusion, extrinsic or intrinsic. In seven of these cases the anatomic conditions were such as to make them peculiarly amenable to surgical treatment. In one the condition was not recognized during life. Six of the patients were operated on, and four survived.

Congenital occlusion of the intestine is most often single and usually complete. The duodenum is the favorite site, except in the event of multiple occlusions, when the jejuno-ileum is most frequently involved. The colon is least frequently affected. When the occlusion is incomplete, there may be a simple narrowing or a perforated diaphragm. When complete there may be absence of a segment, a portion of the bowel may be replaced by a fibrous cord or the lumen may be occluded by a septum.

The bowel above the obstruction is dilated, often extremely so, and the walls are hypertrophied. If the obstruction is above the papilla of Vater, bile will usually be absent, but as was shown by Cordes, bile may be present both above and below the obstruction. Below the obstruction the bowel is wormlike in appearance, usually because it is not distended rather than because it has not developed.

Associated malformations may occur but are not common. The most frequent is anorectal imperforation.

No one theory of the causation of these defects can explain all cases. In the order of frequency (1) developmental defects, (2) fetal accidents and (3) fetal diseases may be mentioned.

The congenital type of volvulus is the result of congenital deficiency in the attachment of the mesentery of the small intestine and lack of fixation of the ascending colon. Violent peristalsis or sudden effort may cause abnormal rotation, partial and recoverable, producing only transient symptoms, or complete and, if unrelieved, fatal.

Symptoms.—Complete atresia is incompatible with life and causes symptoms shortly after birth. When the obstruction is incomplete, particularly when it is situated in the duodenum, the length of life is sometimes surprising.

Vomiting, beginning soon after birth, usually as soon as feeding is begun, is the leading symptom. At first the vomiting may occur only when food is taken but later is persistent and independent of feeding. In the majority of cases the vomitus is bile stained. In the case of stenosis vomiting may be greatly delayed.

The character of the stools depends on the situation of the obstruction. If it is above the opening of the bile duct, typical meconium is passed in varying amounts; if below the papilla, the stools are scanty and usually consist of small amounts of grayish mucus. When the obstruction is incomplete, the stools are at first typical meconium, and are later changed by the small amount of milk which passes the stenosis.

Distention is present in most cases, and the degree is determined by the situation of the obstruction. In cases of duodenal atresia, distention is limited to the upper part of the abdomen. Peristaltic waves may be noted passing from the left to right. Distention of the whole abdomen is noted when the obstruction is lower in the intestine. In such cases irregular peristaltic waves may be seen, and the dilated intestinal coils palpated.

Progressive loss of weight and dehydration are evident. In any case of persistent vomiting in a new-born infant roentgenographic examination is imperative and will usually give definite information as to the presence and site of the obstruction. An opaque meal or enema may be given with safety in the earliest infancy.

In the case of volvulus imposed on abnormal rotation the infant remains apparently normal for a varying period after birth. Meconium is passed and subsequently milk stools. With the onset of volvulus the symptoms are those of duodenal obstruction.

Diagnosis.—The conditions to be differentiated are: Malformation of the anus and rectum; internal hernia with strangulation and pyloric stenosis.

Imperforate anus may be complicated by atresia of the intestine. If, in a case of imperforate anus, the intestinal contents are gray and pasty, it is reasonable to assume the presence of obliteration of the intestinal lumen higher up and below the bile duct. An obstruction of the rectum may usually be demonstrated by digital examination.

The strangulation of an internal hernia would probably be difficult to diagnose unless the hernia were diaphragmatic in which event the thorax would show characteristic signs.

Pyloric stenosis rarely gives rise to symptoms at so early an age and is excluded by the roentgenogram and by the absence of tumor.

Treatment.—In atresia or stenosis, entero-anastomosis is the operation of choice. When the duodenum is involved, duodenojejunostomy is preferred to gastro-enterostomy. Of the four cases in which operation for intrinsic obstruction of the duodenum was performed by me, there were three instances of atresia. In one of these a gastro-enterostomy was done, and the patient died on the twenty-third day as a result of infection of the wound due to an infected umbilicus. In the second case an anterior duodenojejunostomy was performed, and the patient is now 2½ years old. A posterior duodenojejunostomy was performed in a similar case in which the patient was recently discharged. In the fourth case, one of stenosis of the duodenum, a posterior duodenojejunostomy was carried out, and the patient is now 17 months of age.

In the case of volvulus, the intestines should be untwisted and restored to as normal relations as possible. In the one case of this condition observed by me, the volvulus recurred and a second operation was necessary twenty days after the first. This child is now 4 years of age. It is probably desirable to fix the cecum by suture in as nearly normal a situation as possible to prevent recurrence. In the obstructions lower down entero-anastomosis is indicated, possibly with the addition of a temporary enterostomy.

DISCUSSION

DR. JOHN M. HANFORD: I am glad to have had the opportunity to hear Dr. Bolling's paper. Although my experience with conditions covered by Dr. Bolling is limited, I am familiar with some forms of obstruction in children. It is interesting to observe that in the transverse colon where the midgut joins the hindgut during embryonic life obstruction does not often occur.

I suspect that many cases of congenital intestinal anomaly may not become apparent during infancy or childhood but may cause trouble during adolescence or later life. A so-called congenital duodenal band may be an example of this.

Although Dr. Bolling did not discuss imperforate anus in his paper, I would like to take this opportunity to say that usually in these cases it is better to do a loop colostomy than a stab through the perineum. A colostomy, with an opaque material injected into the distal loop, relieves the obstruction. Roentgen-ray studies may reveal details of the proctodeum, which are likely to be helpful in a careful plastic repair of the defect later in life, giving better chance of success.

DR. BOLLING: In closing the discussion I wish merely to emphasize the value of careful roentgen-ray examination of babies who begin to vomit shortly after birth.

A POSSIBLE CAUSAL FACTOR OF FOOD ALLERGY IN CERTAIN INFANTS. DR. BRET RATNER.

This article will be published in full in a later issue.

DISCUSSION

DR. OSCAR M. SCHLOSS: Dr. Ratner has made a commendable effort to explain these obscure cases of allergy which we all encounter. He has attacked the problem from a new point of view, and I think that his theory has a rational basis.

Some years ago I was much interested in this subject with the idea that foreign protein might be excreted in the mother's milk, thereby sensitizing the infant. A number of experiments were conducted by feeding a nursing mother large amounts of cow's milk or egg white, and her milk was tested for the foreign protein by sensitization tests on guinea-pigs. The results were entirely negative. Later Shannon reported positive results using a somewhat different technic. Stuart, however, was unable to confirm Shannon's results. It seems apparent, therefore, that there is no evidence to support this view.

Dr. Ratner's observation that frequently a history is obtained which would indicate that a mother of an infant sensitive to some particular food had over indulged in this food during her pregnancy is confirmed by my own experience. On the other hand, of course, no one has shown that such overindulgence always leads to sensitization of the baby.

If experiments on guinea-pigs can be translated to human beings, Dr. Ratner's observations demonstrate a means by which infants may become sensitized in utero.

Regular Meeting, April 12, 1928

WILLIAM ROPES MAY, M.D., *President, in the Chair*

BODY MECHANICS AS A FUNDAMENTAL FACTOR IN PEDIATRIC PROBLEMS. DR. R. S. HAYNES.

The subject of body mechanics underlies the handling of almost all the problems related to the health, growth and happinesss of children. Faulty action of the various elements of our body creates an obstacle which may determine defeat of whatever we may attempt to accomplish.

The word mechanics is preferable to "posture," because the latter is too static in idea. Not only the position of the body in relation to the vertical must be considered, but the meaning of every detail of outline in terms of the underlying relationship of parts and their interaction must be known.

A complete physical examination must be made, including the functioning of all joints and muscles.

The principal mechanisms to be considered are the lumbar lordosis, the thoracic compression, the position of the head and the standing mechanism in the lower extremities.

There are many types of children for whom correction of body mechanics may be of help.

The relation of diet and digestion to this subject is close. The relation of basic diets, calcium and phosphorus metabolism to this subject is suggested.

The support of the trunk by the lower extremity is active, pushing the trunk away. The foot is still somewhat a cerebral member. Under observation, children

have unconscious movements which reveal an underlying mechanism beginning at the hip joint which causes one to stand correctly.

This mechanism is in its detail identical with the positive supporting reflex in decerebrate animals, and it is undoubtedly the expression of a spinal reflex.

The method of correction illustrated is a harmonizing of cortical control with the reflex patterns existent in all animals.

DISCUSSION

DR. RUSSELL A. HIBBS: I think that those of us who are seeing gross deformities, as many of us do see in the orthopedic clinics, forget the kind of demonstration that Dr. Haynes has given. It is a valuable demonstration of what can be done with those children who are not severely deformed but who are handicapped, and I think that the evidence of the defeat of the handicapped ought to make us realize what these children suffer from slight deformities. I am sure all of us are grateful to Dr. Haynes for his paper. It has opened up a field in which accurate work and careful and intelligent study will give fruitful results. It has already helped us in the Orthopedic Hospital to apply some of these methods in cases in which there are deformed conditions.

DR. A. S. TAYLOR: I do not feel competent to talk on this subject, as a whole, but there are one or two minor points about which I would like to speak. One is particularly in regard to abdominal disturbances due to bad posture. It has been my experience to operate on a considerable number of people — children and adolescents — who have had disturbance at the end of the duodenum (even duodenal ileus), and it is an interesting fact that in nearly all of these people there is a well marked lumbar lordosis, and the terminal duodenum lies in front of the midline of the lumbar spine and the superior mesenteric vessels come down also in the midline instead of to the left of the spine as is normal, so that the duodenum is compressed directly between the vessels and lordotic spine.

It is a fact that in certain of these cases in which the condition has not developed to an extreme degree relief is obtained from the change in mechanism that Dr. Haynes has described. Some have progressed to the point at which the duodenum is not competent to overcome the obstruction, even when the lumbar spine has been straightened, so that operation is necessary.

The other point is in relation to the albuminuria which is said to be common in these children. I think there is another explanation in addition to the "twist in the kidney," which was held responsible. It may have more relation to the albuminuria than a twist in the position of the kidney. It is a fact that the vessels of the left kidney pass beneath the superior mesenteric vessels just at the origin from the aorta, so that the renal vessels are caught in the apex of the angle between the origin of the superior mesenteric vessels in front and the aorta behind, with the terminal duodenum just below and in the same space.

It will readily be seen that any increase in the lumbar lordosis would crowd the aorta forward against the superior mesenteric vessels and thus cause increased compression of both the left renal vessels and terminal duodenum, causing, on the one hand, congestion of the left kidney with albuminuria and, on the other, obstruction of the duodenum with characteristic symptoms.

The specimen of urine taken in the morning shows no albumin, but as the fatigue of the day increases, the lordosis increases, obstruction of renal circulation occurs and albuminuria results.

These conditions can be enormously benefited by the method worked out and presented this evening by Dr. Haynes. It has been my privilege to see a number of children and some adults really made over by Dr. Haynes.

DR. J. L. YOUNG: I have been familiar with Dr. Haynes' work for some years and have been impressed with the necessity of his or similar medical service for many children coming under my care. I believe that the beginning of a great deal of this trouble is to be found in the improper seating in our schools; these children are put in a position which of necessity is bound to interfere with their

proper muscular development, and, unfortunately, the teachers the country over seem to think that a few hours loss of school is worse than losing a leg. Of what benefit is education to any human being without a good physique to make use of it? For the last twenty-three years my work has been mainly with children, and close observation has convinced me that proper body mechanism is essential to bring about normal development of the human body, and this also applies to the normal development of the dental arches.

DR. A. H. CILLEY: I also wish to thank Dr. Haynes for giving us neither "fads nor fancies" but real substance. He evidently does not give exercises which take up half a day and which produce fatigue instead of exercise. Exercise is good, but fatigue is bad. Rest in proper position is also essential. Simple exercises done slowly, as he has shown us, are ideal. A long string of stunts confuses the child, and he accomplishes nothing. Of course, Dr. Haynes does not carry his exercises straight through without rest periods. Do you?

DR. HAYNES: Of course not.

DR. NORTON: I wish to thank Dr. Haynes for an interesting evening spent on a subject of which I have been grossly ignorant.

DR. HAYNES: I agree with Dr. Cilley on the question of making children do difficult things which cause fatigue. I wish he could give me a word to replace "exercises." What I have been trying to do is not to devise a system of exercise in the ordinary sense of the term. I do not so much wish them to make an effort which will produce fatigue, but to create a habit of muscle association. I would like to ask you to forget for the moment the question of method. There may be many methods. I like the one here demonstrated, because I think it has a relation to the normal postural reflexes existent in all animals; but the idea which I hope you will take away with you is that whatever may be our problem as pediatricians, it is a problem in relation to the body of a young human being. Whenever that problem may locate itself, there we encounter the proper or improper mechanics of that part, and if it is good or if we can make it better than it is, our problem has a better chance of successful solution.

Book Reviews

A Text Book of Infectious Diseases. The Third Edition of Goodall and Washbourn's Manual of Infectious Diseases. By E. W. Goodall, O.B.E., M.D., B.S. Price, $10.00. Pp. 718, with 20 plates, 6 colored plates, 15 diagrams, and 34 charts. New York: William Wood & Company, 1928.

In the nineteen years that have elapsed since the second edition of this excellent book was published, a vast amount of work has been accomplished in connection with these diseases. It is remarkable how much of the worth while part of the work has been incorporated into this book in such a readable manner. All of the infectious diseases important to the temperate zone are described fully and with great clearness. The plates and diagrams are clear and well chosen. Six chapters of appendix have been added containing such important discussions as the treatment of anaphylaxis, of cerebrospinal fluid in health and disease, and of lumbar, cisternal and ventricular puncture. This book fills a long felt need. It is remarkable how the latest and best of recent advances in treatment and prophylaxis have been incorporated in the book. It deserves a place in the library of every practitioner.

Clinique Medicale des Enfants. Affections de L'Appareil Urinaire. By P. Nobecourt. Price, 40 francs. Pp. 345. Paris: Masson et Cie, 1927.

Nobecourt discusses the diseases of the urinary tract in children. The volume contains 345 pages, 234 of which are devoted to various forms of nephritis; 34 are given to pyelonephritis, 16 to the malignant tumors of the kidney in children, 18 to orthostatic albuminuria, and the rest of the book is devoted to paroxysmal hemoglobinuria due to chilling, and lithiasis.

The book contains a number of interesting clinical observations, to which, perhaps, more space is devoted than is necessary. A more detailed account of the functional diagnosis is missing. The volume does not concern itself at all with the newer work of trying to elucidate the part the tissues play in fluid exchange of the patient. The pathologic anatomic data is rather meager.

Acute Aplastic Anaemia: Its Relation to a Liver Hormone. By A. Hayes Smith. Price, 6 shillings. Pp. 80, with 3 charts. London: H. K. Lewis & Company, 1928.

The author reports one case of aplastic anemia in which the patient was treated with liver extract. He endeavors to prove that the efficacy of liver in the treatment is due to a powerful hormone, which normally controls the bone-marrow hemopoietic function. The book is divided into two parts; the first deals with the author's own case in detail and the second part is a résumé of the cases reported in the literature, which is used as internal evidence for the presence of this hormone in the liver.

Everyday Problems of the Everyday Child. By Douglas A. Thom, M.D. Price, $2.50. Pp. 344. New York: D. Appleton & Company, 1928.

This book has been written particularly for parents and only such suggestions as to treatment of these everyday problems seen in normal children as are capable of practical application have been given. It is these conditions, however, in which most parents and teachers are interested, and they are discussed in a thorough and understandable manner.

Directory of Pediatric Societies

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SECTION ON DISEASES OF CHILDREN

Chairman: Dr. W. A. Mulherin, 753 Broad St., Augusta, Ga.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Place: Portland, Ore. Time: 1929.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Henry L. K. Shaw, 142 Washington Ave., Albany, N. Y.
Secretary: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.

THE ASSOCIATION OF AMERICAN TEACHERS OF THE DISEASES OF CHILDREN

President: Dr. J. P. Crozier Griffith, 1810 Spruce St., Philadelphia.
Secretary: Dr. Paul W. Emerson, 86 Bay State Road, Boston.

AMERICAN CHILD HEALTH ASSOCIATION

President: Hon. Herbert Hoover, 370 Seventh Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 Seventh Ave., New York.
Place: Stevens Hotel, Chicago. Time: October 15-19, 1928.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. G. R. Pirie, 20 Madison Ave., Toronto.
Secretary: Dr. A. P. Hart, 1844 Bloor St. West, Toronto.

SECTIONAL

CENTRAL STATES PEDIATRIC SOCIETY

President: Dr. H. T. Price, 121 University Place, Pittsburgh.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Ave., Chicago.
Place: Pittsburgh. Time: October 26-27, 1928.

SECTION ON PEDIATRICS OF SOUTHERN MEDICAL ASSOCIATION

Chairman: Dr. E. C. Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. A. J. Waring, De Renne Apts., Savannah, Ga.
Place: Asheville, N. C. Time: November 12-15, 1928.

LOCAL

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. W. L. Channell, Medical Bldg., Oakland, Calif.
Secretary: J. E. Parrott, Medico-Dental Bldg., San Francisco.
Place: Various Teaching Schools. Time: Monthly.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Oscar Reiss, Westlake Professional Bldg., Los Angeles.
Secretary: Dr. William Sidney Bowers, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

THE ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. W. Wiley Jones, Majestic Bldg., Denver.
Secretary: Dr. Berryman Green, 537 Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month, 2:30 p. m., September to May, inclusive.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Joseph Yampolsky, 127 Peachtree St., Atlanta.
Secretary: Nevin M. Atkins, Atlanta.

PEDIATRIC SECTION OF FULTON COUNTY MEDICAL SOCIETY, ATLANTA, GA.

President: Dr. William W. Anderson, 362 Peachtree St., Atlanta.
Secretary: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St., Atlanta.
Time: Second Thursday of each month from October to April, at 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. James Herbert Young, 66 Commonwealth Ave., Boston.
Secretary: Dr. Thomas Lanman, 286 Marlborough St., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Maurice Blatt, 30 N. Michigan Ave., Chicago.
Secretary: Dr. J. K. Calvin, 104 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. L. R. De Buys, 1487 Delachaise St., New Orleans.
Secretary: Dr. F. J. Kinberger, 3601 Prytania St., New Orleans.

DETROIT PEDIATRIC SOCIETY

President: Dr. George E. White, Capitol Theatre Bldg., Windsor, Ontario, Canada.
Secretary: Dr. W. S. O'Donnell, 1563 David Whitney Bldg., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. F. W. Schlutz, University of Minnesota, Minneapolis.
Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Place: University Campus and Rochester. Time: Winter, Spring, Summer, Fall.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Park J. White, Beaumont Bldg., St. Louis.
Secretary and Treasurer: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

NEBRASKA-IOWA PEDIATRIC SOCIETY

President: Dr. Floyd Clarke, 731 City Nat'l Bank Bldg., Omaha.
Secretary: Dr. R. B. Eldredge, 1036 Medical Arts Bldg., Omaha.
Place: Add-Sell Restaurant. Time: Second Thursday of each month from October to May, inclusive, 6 p. m.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Louis M. Ruderman, 961 Eastern Parkway, Brooklyn.
Secretary: Dr. Joseph F. Paulonis, 1357 Bushwick Ave., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

BRONX PEDIATRIC SOCIETY

President: Dr. William Hinz, 1964 Grand Concourse, New York.
Secretary: L. H. Barenberg, 1749 Grand Concourse, New York.
Place: Concourse Plaza, 161st St. and Grand Concourse, New York.
Time: Second Wednesday of each month, except June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady, N. Y.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany, N. Y.
Place: Various Cities in New York. Time: Fourth Thursday of October, January and April.

PEDIATRIC SECTION OF THE NEW YORK ACADEMY OF MEDICINE

President: Dr. Stafford McLean, 17 East 71st St., New York.
Secretary: Dr. Frank Elmer Johnson, 300 West End Ave., New York.
Place: New York Academy of Medicine, 2 East 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

THE PEDIATRIC SECTION OF THE ACADEMY OF MEDICINE OF CLEVELAND

Chairman: Dr. J. W. Epstein, 3912 Prospect Ave., Cleveland.
Secretary: Dr. Charles W. Burhans, 14805 Detroit Ave., Lakewood, O.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

PEDIATRIC SECTION, ACADEMY OF MEDICINE, TORONTO

President: Dr. M. A. Cox, 34 St. Clair Ave. West, Toronto.
Secretary: Dr. F. R. Hassard, 1361 King St. West, Toronto.
Time: November 17, December 15, February 16 and March 15.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Edward L. Bauer, Jefferson Medical College, Philadelphia.
Secretary: Dr. John Porter Scott, 2040 Pine St., Philadelphia.
Place: College of Physicians, 19 S. 22nd St., Philadelphia. Time: Second Tuesday of each month from October to June, inclusive.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. W. D. Blue, 1024 Madison Ave., Memphis, Tenn.
Secretary: Dr. Gilbert J. Levy, 899 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

TEXAS PEDIATRIC SOCIETY

President: Dr. Edwin G. Schwarz, Medical Arts Bldg., Fort Worth.
Secretary and Treasurer: Dr. Ramsey Moore, Medical Arts Bldg., Dallas.
Place: San Antonio. Time: October, 1928.

RICHMOND PEDIATRIC SOCIETY

President: Dr. T. D. Jones, Medical Arts Bldg., Richmond, Va.
Secretary: Dr. W. Ambrose McGee, West End Medical Bldg., 2618 Grove Ave., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St., Richmond, Va.
Time: First Thursday of each month (other than during the summer).

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Lawrence T. Royster, University, Va.
Secretary: Dr. William B. McIlwaine, Petersburg, Va.
Place: Danville, Va. Time: October 17, 1928.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. R. S. Miles, Fidelity Bldg., Tacoma, Wash.
Secretary: Dr. D. M. Dayton, 704 St. Helens Ave., Tacoma, Wash.

SEATTLE PEDIATRIC SOCIETY

President: Dr. George B. McCulloch, Cobb Bldg., Seattle.
Secretary: Dr. C. L. Smith, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, at 7 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. A. B. Schwartz, 418 E. North Ave., Milwaukee.
Secretary: Dr. M. G. Peterman, 167 Seventeenth St., Milwaukee.
Place: Children's Hospital, Milwaukee. Time: Second Wednesday of each alternate month, beginning with February.

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